Prevalence, Traditional medicine use and Co-morbidities among type 2 diabetes mellitus in outpatients - a cross sectional hospital-based survey in KwaZulu-Natal.

Submitted in fulfilment of the requirements for the degree of Master of Health Sciences in Environmental Health

By

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DECLARATION

I, **Lauren Chetty**, declare that the contents of this research project submitted at the Department of Community Health Studies at the Durban University of Technology for a master's degree are my unaided original work, except where specific indication is given to the contrary (by reference). I confirm that it has not been previously submitted for a degree at any Higher Education Learning Institution.

01/ 02/ 2020

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DEDICATION

I dedicate this thesis to:

My parents (Beverly and Trevor Chetty)

My late grandparents (Mr. and Mrs. Lazarus and Mr. and Mrs. Chetty)

And my nieces; (Amelia, Atarah and Paisley)

Throughout my life, my family has been my strength and source of motivation and inspiration. This dissertation is symbolic of what we as a family have accomplished.

This one belongs to us!

“With God all things are possible”

Mathew 19: 26

LIST OF PUBLICATIONS

This dissertation is based on the following papers that have been published or under consideration for publication.

Published manuscript

1. **Chetty L**, Govender N, Govender GM, Reddy P. Demographic stratification of Type 2 diabetes and comorbidities in district healthcare in KwaZulu-Natal. S Afr Fam Pract. 2021; 63(1), a5218. https://doi.org/10.4102/safp.v63i1.5218

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CONFERENCE PRESENTATIONS

1. National/regional conference

Oral presentation at the KwaZulu-Natal department of health research day 2021.

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ABSTRACT

Throughout the world, diabetes mellitus (DM) affects people of all ages, irrespective of gender and ethnicity, and impacts both rural and urban areas, as well as developing and developed countries. The prevalence of DM in sub-Saharan Africa is a significant public health burden which is attributed to inadequate health care funding, limited medicinal access and the disproportionate provision of resources between private and public health care. Approximately 451 million adults worldwide have diabetes, with predictions of 693 million cases by 2045. Moreover, Type II diabetes mellitus (T2DM) accounts for approximately 90% of diabetics, making it the most common type. Premature morbidity and mortality are associated with it, leading to micro- and macrovascular complications. There is a growing trend for patients to use traditional medicine (TM) commonly known as complementary and alternative medicine in most countries, in an attempt to eliminate or minimize the consequences of their illnesses and improve their general health. Therefore, this study aimed to determine the prevalence and, extent of traditional medicine use and co-morbidities among T2DM in a regional hospital in KwaZulu-Natal. This was a quantitative and cross-sectional study made up of 2 phases. Phase 1 was based on a retrospective chart review of all outpatients who were treated for T2DM between August 2018- January 2019. Demographic data and existing comorbidities were obtained from the hospital registers. Phase 2 involved the prospective recruitment of participants using a structured questionnaire, to determine their use of home remedies/ traditional medicine for T2DM and their co-morbidities thereof.

Data from phase 1 revealed significantly more female patients (3072) compared to male patients (1050) ($p<0.001$). Majority of the outpatients (77.42%) presenting with T2DM over the 6-month period were between the ages of 45 years and 74 years. There was a significant correlation between Indian female patients who presented with T2DM compared with African female patients ($p<0.05$). The more frequent comorbidities experienced by patients were hypertension (3212) and cardiovascular problems (460) with a prevalence of 77.9% and 11.16%, respectively. The likelihood of presenting with comorbidities increased significantly with age. Logistic regression test found that female patients with T2DM were at significantly higher risk of presenting with hypertension (odds ratio [OR] = 1.44, 95% CI:1.20;1.71), arthritis (OR = 2.20, 95% CI:1.51;3.20) and anaemia (OR = 2.42, 95% CI:1.40;4.19), whilst their risk for cardiovascular problems was

significantly lower compared to male patients (OR = 0.67, 95% CI: 0.54;0.83). The results obtained in phase 2 indicated that out of a total of 340 participants (n=244) included, 72% of them were female. T2DM was most prevalent in those aged 45 to 59 (47.94%). Out of 340 participants, only 92 (27%) used TM most often, with Indians (58.24%) being the most frequent users. Nearly 78 % of patients (n = 101) were using TM in conjunction with hospital medication. Families and friends were the most common sources of TM knowledge. Lemon and honey, Aloe vera, bitter gourd or karela, green tea, cinnamon, curry leaves and tulsi leaves were reported as the most commonly used TM. Traditional medicine use was predicted by various factors, including gender, race, age, education, residence, and presence of DM, however, no significant predictors for TM usage was noted among the variables tested. Traditional medicine use among African participants was 0.56 times (OR=0.56, 95% CI=0.34, 0.93), lower than that of Indian participants.

Demographic factors, such as gender, ethnicity, and age, influenced the prevalence of T2DM and comorbidities. To allocate medical resources effectively and according to the true burden of disease from complications caused by T2DM, flexible and adaptive approaches are needed for prevention and management of T2DM cases. Furthermore, the study highlighted a low prevalence rate of TM usage (27.06%) in T2DM patients. Traditional medicine was predominately used among females and ethnicity was found to be a significant predictor of TM usage. The data from this study can be used to develop a tracking system, which will inform the health care systems with current information and may reduce the exponential rise of the number of patients suffering from DM. Future research is needed to determine if herbal therapies are effective therapeutic options in managing T2DM due to their safety and multiple targeting effects. Traditional medicine/ home remedies may be more effective in the development of anti-diabetic drugs if systematic data regarding their structure, activity, and mode of action is collected.

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LIST OF ABBREVIATIONS

BMI	-	Body mass index
CAM	-	Complementary alternative medicine
CAT	-	Complementary alternative therapy
COVID-19	-	Coronavirus disease
CVD	-	Cardiovascular disease
DM	-	Diabetes Mellitus
EMME	-	Eastern Mediterranean and the Middle East
GAD65	-	Glutamic acid decarboxylase
GD	-	Gestational diabetes
IAAS	-	Insulin auto-antibodies
ICA'S	-	Islet cell antibodies
IDF	-	International diabetes federation
KZN	-	KwaZulu-Natal
LMIC	-	Low middle-income country
NCD’s	-	Non-Communicable diseases
OR	-	Odds Ratio
SA	-	South Africa
SAFPJ	-	South African Family Practice Journal
SANHANES	-	South African National Health and Nutrition Examination Survey
SES	-	Socioeconomic status
SSA	-	Sub-Saharan Africa
T1DM	-	Type 1 diabetes mellitus
T2DM	-	Type 2 diabetes mellitus
TCAM	-	Traditional and complementary alternative medicine
TM	-	Traditional medicine
UK	-	United Kingdom
US	-	United States
WHO	-	World Health Organisation

DEFINITIONS

Acupuncture: A system of complementary medicine in which fine needles are inserted in the skin at specific points along what are considered to be lines of energy (meridians), used in the treatment of various physical and mental conditions.

Aetiology: The cause, set of causes, or manner of causation of a disease or condition.

Aromatherapy: The use of aromatic plant extracts and essential oils for healing and cosmetic purposes.

Cardiovascular disease: A type of disease that affects the heart or blood vessels

Communicable diseases: An illness caused by an infectious agent or its toxins that occurs through the direct or indirect transmission of the infectious agent or its products from an infected individual or via an animal, vector or the inanimate environment to a susceptible animal or human host.

Comorbidities: A disease or medical condition that is simultaneously present with another or others in a patient.

Demographics: The statistical data of a population, especially those showing average age, income, education, etc.

Diabetes mellitus: It is a chronic, metabolic disease characterized by elevated levels of blood glucose

Diabetic retinopathy: A complication of diabetes that affects the eyes.

Ethnicity: The fact or state of belonging to a social group that has a common national or cultural tradition.

Genetics: The study of heredity and the variation of inherited characteristics.

Gestational diabetes: A condition characterized by an elevated level of glucose in the blood during pregnancy, typically resolving after the birth.

Glucose intolerance: Metabolic conditions which result in higher-than-normal blood glucose levels.

Hyperglycaemia: An excess of glucose in the bloodstream

Hypertension: A condition in which the force of the blood against the artery walls is too high.

Incidence: A measure of the probability of occurrence of a given medical condition in a population within a specified period of time.

Indigenous: Originating or occurring naturally in a particular place.

Insulin secretion: The interaction of nutrients, hormones, and the autonomic nervous system.

Insulin: A hormone produced in the pancreas by the islets of Langerhans, which regulates the amount of glucose in the blood.

Ketoacidosis: A serious diabetes complication where the body produces excess blood acids (ketones).

Macrovascular complications: Disease of the large blood vessels, including the coronary arteries, the aorta, and the sizable arteries in the brain and in the limbs.

Microvascular complications: They are long-term complications that affect small blood vessels which include retinopathy, nephropathy, and neuropathy.

Morbidity: Refers to having a disease or a symptom of disease, or to the amount of disease within a population

Mortality: Is a measure of the number of deaths in a particular population

Nephropathy: A medical term for kidney disease

Neuropathy: Disease or dysfunction of one or more peripheral nerves, typically causing numbness or weakness

Non-communicable diseases: Is medical conditions or diseases which by definition is non-infectious and cannot be passed from person to person.

Normoglycaemia: The presence of a normal concentration of glucose in the blood.

Prevalence: It is the proportion of a particular population found to be affected by a medical condition at a specific time

Traditional medicine: The knowledge, skills and practices based on the theories, beliefs, and experiences indigenous to different cultures, used in the maintenance of health and in the prevention, diagnosis, improvement, or treatment of physical and mental illness.

Type 1 diabetes mellitus: A chronic condition in which the pancreas produces little or no insulin.

Type 2 diabetes mellitus: A chronic condition that affects the way the body processes blood sugar (glucose).

Vasoconstriction: The narrowing of blood vessels by small muscles in their walls.

CHAPTER ONE

1.1. Introduction

Non-communicable diseases (NCDs) such as diabetes mellitus (DM) is a major health care and economic burden. Diabetes mellitus is increasing at an alarming rate worldwide, especially in developing countries (Pillay, Lutge and Aldous, 2016). The increasing prevalence of DM in sub-Saharan Africa (SSA) remains a challenge because of inadequate funding, limited medicinal access and the disproportionate resources between private and public health care. Moreover, the increase in prevalence is due to an epidemiological shift toward life styles that promote sedentary, unhealthy habits, improved survival rates and aging populations, and enhanced detection and diagnosis (Elhendi, 2015). Type II diabetes mellitus (T2DM) influences morbidity and mortality both in SSA (Hall, Thomsen, Henriksen and Lohse, 2011) and South Africa (SA) (Pheiffer *et al*., 2018). An estimated 50% of DM cases worldwide are undiagnosed, with the most arising in low- and middle-income countries (Pheiffer *et al*., 2018).

In SA, the prevalence of DM is rapidly increasing, with almost 2 million (9%) people aged 30 years and older being diagnosed since 2012, an increase of 3.5% since 2000 (Pheiffer *et al*., 2018 and Peer *et al*., 2012). Demographic factors such as age, sex, ethnicity, economic status, and urbanization associated with nutrition transition and obesity also play a significant role in increased prevalence (Pheiffer *et al.,* 2018). In KwaZulu-Natal (KZN), a prevalence of more than 12% was reported amongst the Indian population (Sahadew, Singaram and Brown, 2016). Likewise, in Cape Town, the prevalence of DM among 1099 African participants was 13.1% and considerably higher than previous reports (Peer *et al.*, 2012). The rising DM prevalence across SA adds to the current chronic disease burden and thus warrants the need to investigate this elevation amongst the African population. In contrast, an estimated 25.8 million people living in the United

States (US), are diagnosed with DM, of which 8.4% are American Indians and 12.6% are African American population (Spanakis and Golden, 2013).

Traditional medicine (TM) use is a popular mode of treatment amongst those diagnosed with DM (Chege, Okalebo, Guantai, Karanja, and Derese, 2015), especially among those living in developing countries (Frimpong and Nlooto, 2018). In the US, almost 40% reported TM use compared to 52.79% of South Africans (Frimpong and Nlooto, 2018). Notably, 80% of SSA's population report TM as their primary mode of health care management (Keter and Mutiso, 2012). Despite the reduction in side effects, cost-effectiveness, and easier accessibility of TM in controlling DM and its associated complications (Ching, Zakaria, Paiman and Jajalian, 2013; Chang, Wallis, and Tiralongo, 2012 and Ahwinahwi and Chukwudi, 2016); severe health complications were reported in a Dubai population, when used with conventional medical treatments, or when conventional treatments are completely abandoned in favor of TM (Alalami, Saeed and Khan, 2017). Kaburi (2017) also support the theory that TM use reduces compliance with conventional medicine, resulting in chronic complications and/or comorbidities (Kaburi, 2017).

Chronic complications associated with T2DM imposes a huge economic burden on the health care system, reduces the patient's quality of life, and consequently increase diabetic mortality (Liu, Fu, Wang, and Xu, 2010). Patients with uncontrolled T2DM are more likely to develop micro- and macro-vascular conditions (Liu *et al*., 2010 and Deshpande, Harris-Hayes and Schootman, 2008), predisposing them to cardiovascular disease, diabetic retinopathy, diabetic neuropathy, and diabetic nephropathy (World Health Organization (WHO), 2016). In light of the geographical differences and the increase in economic burden associated with T2DM, flexible and adaptive management approaches are necessary (Liu *et al*., 2010).

1.2. Rationale

This study was conducted in a regional and district hospital, which is located in a suburb in the eThekwini health district (Figure 1). The hospital has grown from being a community hospital to one of the four major hospitals in the Durban region. The hospital services mainly the poorest Indian and African communities and has a catchment population of over 1500 000 people living in the eThekwini region (KZN Department of Health 2019). In South Africa, approximately 4.5 million people are living with DM as of 2020 (International Diabetes Federation (IDF), 2020), however, this estimation doesn't reflect the impact of gender and ethnicity associated with the current burden of disease. According to Rampersad, Rangiah and Kendon (2019), DM is common amongst all race groups with the highest prevalence amongst the Indian population (15.8%), followed by the African (4.8%) and White (3.5%) populations. There is paucity of DM data amongst the African population in SA, hence, the data derived from this study will improve the current knowledge of the burden of DM amongst these vulnerable populations.

Demographic factors such as age, gender, ethnicity, socio-economic status and urbanization that are associated with nutrition transition and obesity are directly related to the increased prevalence of DM (Pheiffer *et al*., 2018). Earlier reports indicate significant associations between demographic factors and TM use (Ching, Zakaria, Paiman and Jajalian, 2013 and Khalaf and Whitford, 2010). Whilst TM contributes to almost 85% of health care in Africa (Ogbera, Dada, Adeleye and Jewo, 2010 and Ching, Zakaria, Paiman and Jajalian, 2013) and provides symptomatic relief of health issues such as pain disorders, DM, high blood pressure, depression, etc. (WHO, 2021), it negatively affects the patient's health when used together with conventional treatments, or when used independently (Alalami, Saeed and Khan, 2017). Chronic complications together with micro- and macro-vascular conditions, follow closely with the onset of T2DM (Liu *et al*., 2010; Deshpande, Harris-Hayes and Schootman, 2008). Despite the availability of summary data in this regional hospital under study, limited statistical analyses has been done in terms of stratifying new cases by demographics or evaluating co-morbidity risks. Furthermore, chronic complications associated with T2DM influences

the quality of life of the patient. Therefore, evaluating epidemiological data will improve disease monitoring and enable the discourse regarding the social and health implications as well as develop interventions that enhance patient management.

It is important to improve DM data collection by health care systems in order to advance the prediction of incidence, complications, mortality, and the frequency of atypical variants (Pastakia *et al.,* 2017). Thus, this study aimed to determine the demographic profile related to prevalence, extent of TM use and co-morbidities among T2DM patients in this regional hospital in KwaZulu-Natal.

1.3. Research problem

Diabetes mellitus, one of the major NCD's experienced in SA, is characterized by an upward prevalence trend especially amongst the African population. The use of TM for the management of DM has increased significantly, however, this practice may impact on conventional management by increasing comorbidities related to DM.

1.4. Aim

To determine the prevalence and, extent of Traditional medicine use and Co-morbidities among type 2 diabetes mellitus in a regional hospital in KwaZulu-Natal.

1.5. Objectives

1. To determine the prevalence of type II diabetes mellitus between August 2018 – January 2019 in a regional hospital in KZN.
2. To assess the use of traditional medicine among diagnosed type II diabetic patients in a regional hospital.
3. To determine the extent of diabetes related complications and/or co-morbidities among patients with pre-existing type II diabetes mellitus.

1.6. Dissertation structure

This dissertation comprises of 5 chapters. Chapter one provides an introduction, a rationale as well as the aim and objectives of the study. Chapter two provides a comprehensive literature review. The methodology which includes a detailed outline of the study population, data collection and data analysis can be found under chapter three.

Chapter four addresses objectives 1 and 3, which focuses on determining the demographic prevalence of T2DM and existing comorbidities. This chapter entitled “Demographic stratification of Type 2 diabetes and comorbidities in district healthcare in KwaZulu-Natal”, has been published in the South African Family Practice journal (SAFPJ) in 2021. The published manuscript is included.

Chapter five addresses objective 2 and aimed to evaluate the use of TM in patients with T2DM who are on chronic therapy and assess their self-care practices This chapter is presented in manuscript format and is currently under review in the “Advances in Public Health journal’’ (Manuscript number: 7334080) (Annexure A: Proof of submission).

Chapter five provides a synopsis of the discussion derived from both manuscripts and provides a conclusion to the aim and objectives of this study as well as recommendations.

CHAPTER TWO

Literature Review

1. Introduction

According to the 2011 WHO Global Status Report, of the 57 million annual global deaths, a staggering 36 million (> 63%) are attributed from chronic diseases (WHO, 2011). Noncommunicable diseases (NCDs), viz., cardiovascular disease, cancer, diabetes, and chronic respiratory diseases are the 4th leading cause of mortality worldwide, accounting for 1.7, 7.6, 4.2 and 1.3 million deaths respectively, based on the 2011 global epidemiology data. The WHO further estimated that by 2020, global deaths due to chronic diseases are projected to increase by at least 15-20%. It was predicted that these NCDs maybe responsible for 75% of global deaths by 2030, suggestive of an impending disaster for health and society, particularly in low and middle-income countries (LMICs) (WHO, 2011).

Noncommunicable diseases are a major challenge on the already burdened healthcare system. All countries, irrespective of their economic developmental, epidemiological, and demographical variability, are facing an increasing burden of NCDs including diabetes mellitus (DM) (Animaw and Seyoum, 2017). Diabetes mellitus has a devasting impact on both patients and the global economy (Pillay, Lutge and Aldous, 2016). An estimated 50% of diabetes cases worldwide are undiagnosed, with the most arising in LMICs (Pfeiffer *et al*., 2018). The prevalence of DM in sub-Saharan Africa is a significant public health burden because of inadequate health care funding, limited medicinal access and the disproportionate provision of resources between private and public health care (Pastakia *et al*., 2017). Type II diabetes mellitus (T2DM) influences both morbidity and mortality both in SSA (Lee *et al*., 2016) and SA (Pheiffer *et al*., 2018).

2. Definition and classification of diabetes mellitus

Diabetes mellitus is defined as a chronic, lifelong disease, caused by the deficiency or resistance of the hormone insulin which regulates the blood glucose levels (Elhendi, 2015). Moreover, DM describes a variety of disparate metabolic disturbances, the most common of which is chronic hyperglycemia (Kerner and Brückel, 2014; Solis-Herrera *et al*., 2018). The high blood glucose concentration is caused either by impaired insulin secretion, impaired insulin action or both (Kerner and Brückel, 2014). Most cases of diabetes can be broadly classified into 2 categories: type 1 diabetes mellitus (T1DM) and T2DM.

2.1. Type 1 diabetes mellitus

Various studies have indicated that T1DM results from the destruction of pancreatic beta cells by T cells of the immune system (Atkinson, Eisenbarth and Michels, 2014; Burrack, Martinov and Fife, 2017 and Solis-Herrera *et al.,* 2018). In 90% of individuals, markers of immune destruction of the beta-cell exist at diagnosis and contain the islet cell antibodies (ICAs), glutamic acid decarboxylase (GAD65) antibodies, tyrosine phosphatases IA-2 and IA-2b antibodies, ZnT8 antibodies, and insulin auto-antibodies (IAAs) (Skylar *et al*., 2017). Individuals may revert to negative if only one marker is positive, however, an individual's risk of developing T1DM increases with the number of positive markers (DiMeglio, Evans-Molina and Oram, 2018 and Skylar *et al*., 2017). Predictor tests with two positive antibodies are associated with a 75% likelihood of developing DM in the next 10 years (Skylar *et al*., 2017). Type 1 diabetes mellitus can occur at any age but is more prevalent in children and adolescents (Chiang *et al*., 2018 and Kahanovitz, Sluss and Russel, 2017). Younger individuals on average have a rapid rate of beta-cell destruction and present with ketoacidosis, whereas adults often maintain sufficient insulin secretion to prevent ketoacidosis for many years (Kahanovitz, Sluss and Russel, 2017). Notably, approximately 50%-60% of those with T1DM are under 18 years of age at diagnosis, with the disease occurring throughout adulthood but at a lower incidence (Kyvik *et al*., 2004). However, Niba (2016) reported that T1DM accounts for almost 5%-10% of all diabetes cases, with approximately 40% of the patients diagnosed before the age of 20 (Niba,

2016). In contrast, T2DM is more prevalent in adults, albeit a growing incidence among children and adolescents (WHO, 2016).

2.2. Type 2 diabetes mellitus

Type 2 diabetes mellitus is a more common metabolic disorder than T1DM and is responsible for approximately 90 % of all diabetes (Hameed *et al.,* 2015; Goyal, 2018 and Galicia-Garcia *et al*., 2020), particularly in LMICs (WHO, 2019). It is characterized by defective insulin secretion by pancreatic β-cells and the inability of insulin-sensitive tissues to react appropriately to insulin (Galicia-Garcia *et al*., 2020). Additionally, T2DM is referred to as an insulin-resistance condition associated with beta-cell dysfunction, in which there is an initial compensatory increase in insulin secretion, that maintains the normal range of blood glucose levels (Goyal and Jialal, 2018). However, as T2DM advances, the biological function of beta cells are altered, resulting in inadequate insulin secretion and consequent hyperglycemia (Goyal and Jialal, 2018). Most T2DM patients are obese or have a higher body fat percentage particularly in the abdominal region. Excess body fat stimulates insulin resistance through various inflammatory mechanisms, including increased free fatty acid release and adipokine dysregulation (Goyal and Jialal, 2018).

Interestingly, Solis-Herrera *et al*. (2018) presented a sophisticated analyses of the beta-cell response and its regulation, highlighting that most subjects at risk for developing T2DM are those with both impaired fasting glucose and/or impaired glucose tolerance (Solis-Herrera *et al*., 2018). Moreover, these individuals demonstrate an approximate 80% reduction in their total insulin secretory capacity of the pancreas. Most people with T2DM do not require insulin treatment to survive, however, insulin may be needed to prevent chronic complications (Home *et al.,* 2014). Type 2 diabetes mellitus has a latent, asymptomatic period of sub-clinical stages which often remains undiagnosed for many years since the hyperglycaemia is not severe enough to produce noticeable diabetic symptoms (Ramachandran, 2014 and WHO, 2019).

The classification of diabetes together with the etiological types of DM and the clinical stages are illustrated in Figure 1. People with diabetes, irrespective of type, can progress through several clinical stages, extending from normoglycaemia to severe hyperglycaemia with ketosis (WHO, 2019). However, not all diabetic individuals will demonstrate all stages of the disease, whereas individuals with T2DM may move progress from one stage to another in either direction (WHO, 2019). People who have, or who are developing DM can be grouped by stages according to clinical characteristics, in the absence of information concerning the underlying aetiology.

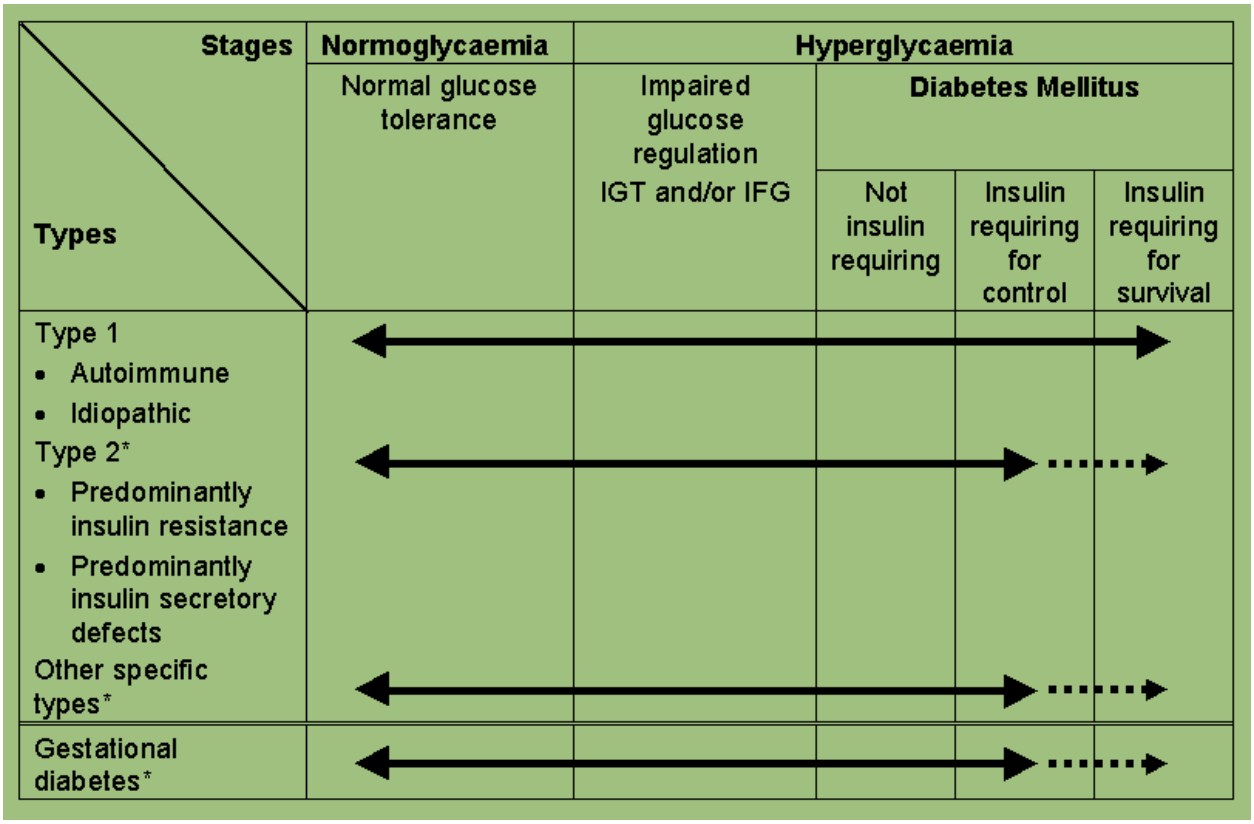

Figure 1: Disorders of glycaemia based on aetiological types and clinical stages (Source: WHO, 2019)

3. Prevalence of type 2 diabetes mellitus

Globally, 422 million adults were estimated to be living with diabetes in 2014 and has almost quadrupled since 1980; and the estimated global prevalence has nearly doubled

since then (Petersmann *et al*., 2018). The global prevalence increased from 1990 (211.2 million) to 2017 (476 million), an increase of 129.7% as illustrated in figure 2 (Lin *et al*., 2020). According to the IDF (2015), the degree of variability for T2DM prevalence globally is quite high. Statistics have shown that East Asia, South Asia, and Australia have a higher number of adults with diabetes than any other region (153 million), however, North America and the Caribbean have the highest prevalence rate, with one in eight affected (IDF, 2015).

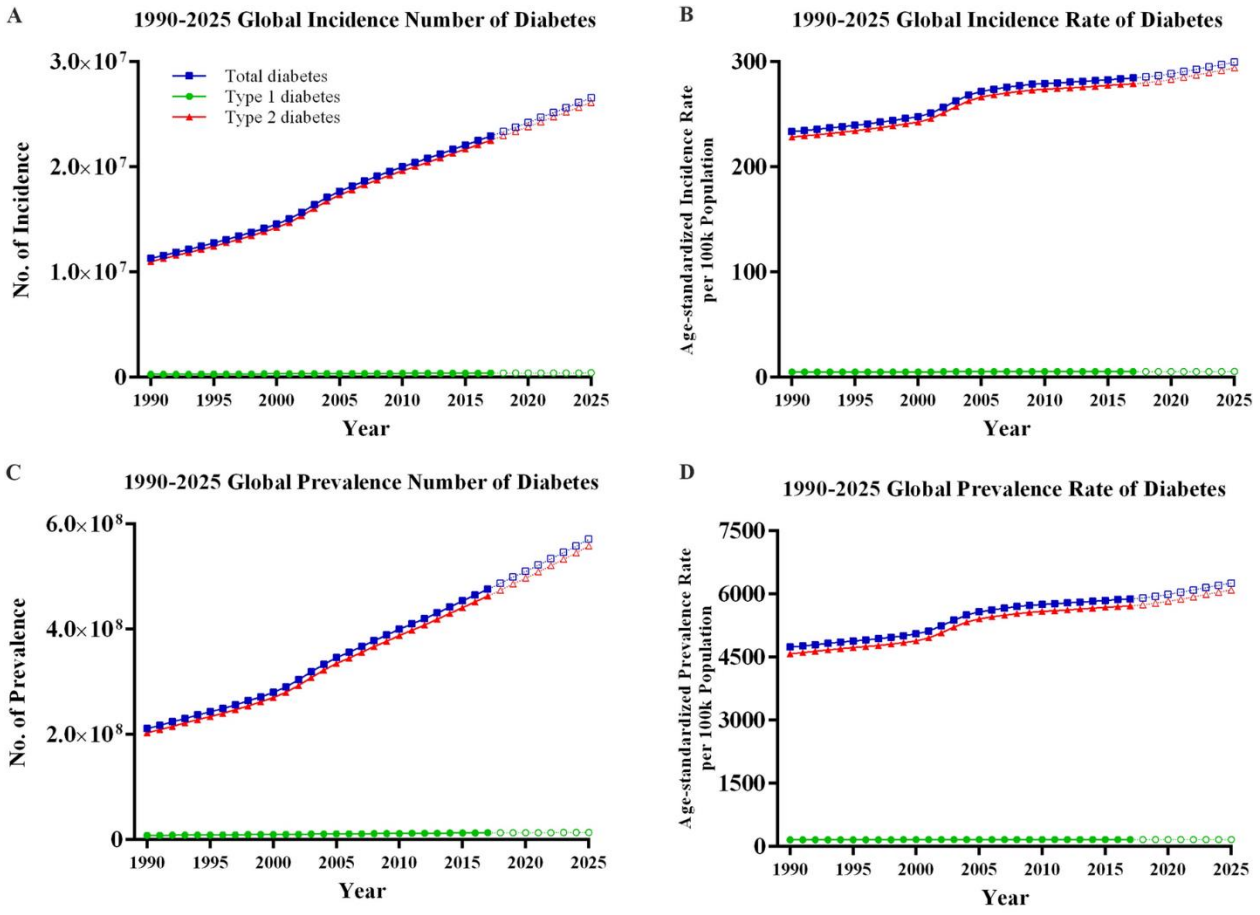

Figure 2: Global incidence and prevalence of DM from 1990 to 2025 (Source: Lin *et al.,* 2020).

Similarly in the US, the National Center for Chronic Disease Prevention and Health Promotion (2020) estimated that more than 34 million people have been diagnosed with diabetes and approximately 88 million have prediabetes (National Center for Chronic

Disease Prevention and Health Promotion, 2020). These findings are comparable to the national disease report from 2014, whereby it was projected that 95% of the nearly 30 million people are living with diabetes and have T2DM and an additional 86 million had prediabetes (Centers for Disease Control and Prevention, 2014). Between 2014 and 2020, a rise in the prevalence of diabetes has been observed, suggestive that prediabetes is a risk factor for T2DM (National Center for Chronic Disease Prevention and Health Promotion, 2020 and Centers for Disease Control and Prevention, 2014). Obesity, being 45 years or older, and infrequent exercising are identified as risk factors for prediabetes and consequent T2DM development (National Center for Chronic Disease Prevention and Health Promotion, 2020 and Centers for Disease Control and Prevention, 2014). The prevalence of T2DM in the US is greater for males (6.9%) than for females (5.9%) (Centers for Disease Control and Prevention, 1980-2014). In the US alone, the total number of Americans suffering from diabetes has increased from 23.6 million in 2007 to 25.8 million at the start of 2011 (Centers for Disease Control and Prevention, 2011). Several factors are implicated, including rapid cultural, economic, and social changes, ageing populations, increasing and unplanned urbanization, dietary changes such as increased consumption of highly processed foods and sugar sweetened beverages, obesity, reduced physical activity, unhealthy lifestyle and behavioural patterns, fetal malnutrition, and increasing fetal exposure to hyperglycaemia during pregnancy (WHO, 2019; American Diabetes Association, 2012 and Hu, 2011).

Calculations of the burden of diabetes is vital in order to distribute community and health resources, as well as to promote healthy lifestyles (Shaw, Sicree and Zimmet, 2010). The diabetes prevalence on a national level for 216 countries for 2010 and 2030 was established using an epidemiological study, that included a combination of studies from 91 countries (Shaw, Sicree and Zimmet, 2010). The highest regional prevalence for 2010 was North America, followed by the Eastern Mediterranean and the Middle East (EMME) and South Asia respectively. The African region is expected to have the largest proportional increase in the prevalence of adult diabetes by 2030, followed by the EMME, albeit, North America will continue to have the world's highest prevalence (Shaw, Sicree

and Zimmet, 2010). It was further predicted that all regions will have an upsurge in numbers of the adult population, hence, the probability of the total numbers with diabetes are most likely to increase by 50% over the next 2 decades (Shaw, Sicree and Zimmet, 2010). Out of the top 10 highest prevalence in the world, 5 of them occur in the Middle East, with a marked difference between developed and developing countries (Shaw, Sicree and Zimmet, 2010). In developing countries, the prevalence is expected to increase by 69% from 2010 to 2030 as compared to developed countries which is expected to rise by 20%. A 54% increase of the overall prevalence of diabetes was predicted from 2010 to 2030, at an annual growth of 2.2%, which is nearly twice the annual growth of the total world adult population (Shaw, Sicree and Zimmet, 2010).

The IDF (2017) estimates that 451 million adults worldwide had diabetes, with projections of 693 million cases expected in 2045. However, according to the IDF (2019), 4.2 million deaths occurred due to diabetes and 463 million adults aged between 20 and 79 years old were living with diabetes and is likely to increase up to 700 million people by 2045 (IDF, 2019). Notably, the highest number of adults presenting with diabetes were aged between 40 and 59 years old (WHO, 2019). Geographical regions are also related to T2DM prevalence, with more than 80% of patients living in LMICs, posing additional challenges for more effective treatment (Islam *et al*., 2014 and Dagenais *et al*., 2016). Despite advances in health care, diabetes remains a major cause of premature mortality, mainly due to associated cardiovascular disease (CVD), with an estimated 4.8 million deaths worldwide attributable to diabetes (Roglic, 2010). The epicenter for the DM epidemic is Asia, which is responsible for more than 60% of this global burden (IDF, 2017 and Hu, 2011). India was reported as the country with the second highest number of people (69.2 million) experiencing T2DM worldwide alongside China (Vijayakumar, 2019). In Africa, the proportion of undiagnosed diabetes is estimated at 69.2% and 77% of deaths due to diabetes occurred in individuals younger than 60 years of age (IDF, 2017). As in other parts of the world, T2DM embodies over 90% of diabetes cases in Africa (Hall *et al*., 2011).

There is a paucity of prevalence data on T2DM from Africa to draw comparisons with the rest of the world (Olokoba, Obateru and Olokoba, 2012). Studies examining data trends within Africa show evidence of a drastic increase in prevalence in both formal and informal setting and affecting both genders equally (Mbanye, 2010). The burden in Africa is mostly caused by T2DM, with less than 10% of diabetes cases being T1DM (Olokoba, Obateru and Olokoba, 2012). This prevalence is anticipated to double by the year 2040 with an upsurge in numbers in Sub-Saharan Africa. The staggering numbers excludes the estimated 62% of people that are undiagnosed in Africa (Olokoba, Obateru and Olokoba, 2012). This increase in prevalence is also believed to be influenced by western lifestyles and poor dietary habits and consequent obesity and DM (Olokoba, Obateru and Olokoba, 2012). The upward trend in DM prevalence is thought to be fueled by the emergence of additional factors such as environmental factors and the increased life expectancy as a result of improved pharmacotherapy (Prakaschandra, 2016). Based on the South African mortality statistics, DM related mortality had the second highest increase following the 5.4% death rate from HIV infections between 2004 and 2005 (Statistics South Africa, 2017 and Chamnan *et al*., 2011). A comparison made by the IDF (2011) between Africa and other continents, confirm that Africa has the lowest diabetes prevalence; the highest percentage of undiagnosed cases and the highest mortality rates due to diabetes complications (IDF, 2011).

South Africa had an adult population close to 59 million according to the 2019 mid-year population estimates (Statistics South Africa, 2019) and 4.5 million people diagnosed with diabetes and a further 2 million people undiagnosed with diabetes (IDF, 2019). Peer *et al*. (2012) claimed that the prevalence of diabetes in South Africa is increasing over time. Using a study of urban, black South Africans, they further stated that the prevalence increased from 8.0% in 1990 to 12.2% between 2008 and 2009 (Peer *et al*., 2012). On the other hand, the IDF (2015) declared that the actual prevalence of diabetes in South Africa, as well as the magnitude of unmet need for diabetes care, remains unclear, as prior estimates for South Africa are largely based on self-reported data, which do not

capture undiagnosed cases and often come from sub-national samples and/or pooled estimates drawing on data from multiple countries.

The prevalence of diabetes in a South African adult population was shown to be greater in women as compared with men (10.7% versus 9.7%) (Stokes *et al.,* 2017). The likelihood of being unscreened was also slightly higher in women (46.3%) than in men (44.0%), while the likelihood of being treated but uncontrolled was higher in men than in women (30.1% of men with diabetes were treated but uncontrolled compared to 15.1% of women with diabetes) (Stokes *et al.,* 2017). Moreover, women with diabetes were more likely to have controlled blood sugar than men (22.8% versus 8.3%) (Stokes *et al.,* 2017). In terms of ethnicity, the prevalence of diabetes was higher in the non-white population, particularly among Indians. The proportion unscreened was also higher in non-whites compared to whites; 54.1% in Africans, 38.4% in the Colored population and 14.4% among Indians/Asians/others, compared to 7.6% of white South Africans (Stokes *et al.,* 2017). Even though the study found that the prevalence of diabetes was highest in those living in urban formal areas, the proportion unscreened was lower in urban formal areas than in other settings (40.4% compared to 68.1% in urban informal areas and 65.1% in rural informal areas) (Stokes *et al*., 2017).

Peer *et al*. (2012) conducted a diabetes prevalence study amongst adults in a predominantly black residential area of Cape Town, in an attempt to compare the results with the results from a study conducted by Levitte and team in 1990. The target population was 25- to 74-year-old residents from 5 different areas in Cape Town (Langa, Guguletu, Crossroads, Nyanga and Khayelitsha). The crude and age-standardized prevalence of diabetes was 12.1% (95% (CI): 10.2–14.0) and 13.1% (95%CI: 11.0–15.1), respectively, with higher rates found in women (crude: 13.8% (95%CI: 11.4–16.3); age-standardized: 14.7% (95%CI: 12.1–17.3)) compared to men (crude: 10.2% (95%CI: 7.1–13.4); age-standardized: 11.3% (95%CI: 8.0–14.6)). The prevalence of unknown diabetes was 4.9% with similar rates in men (4.8%) and women (4.9%). However, the rate of known diabetes (7.2%) was lower in men (5.4%) compared to women (8.9%) (Peer *et al*., 2012).

Low-income countries of Sub-Saharan Africa, including Uganda have the fastest growing rates of DM, whereby the diabetes population has significantly increased from an estimated 98,000 patients in 2000 to approximately 1.5 million in 2010 from a population of 30 million people (Nyanzi, Wamala, and Atuhaire, 2014). Despite the increase in diabetes burden, interventions are still poor and epidemiological data are scarce. There are no national noncommunicable disease surveys in Uganda, so information is very limited (Nyanzi, Wamala, and Atuhaire, 2014). The prevalence rate of diabetes was 65% in the 61–65-year age group, followed by 30.4% among the 51-55 years group (Asiimwe, Mauti and Kiconco, 2020). A systematic review analyses conducted by Bertram and coworkers, aimed to identify the prevalence and mortality rates for diabetes in South Africa, between 1990 to 2013, using community-based studies and the revised WHO criteria (Bertram *et al.,* 2013). The total prevalence of T2DM in those over age 30 was estimated at 9.0% (7.4% in men and 10.4% in women). A considerable increase of 5.5% in prevalence was noted (Bradshaw *et al*., 2000). It is estimated that about 1 million people with T2DM in South Africa are undiagnosed (Bertram, 2013).

Diabetes caused more than 25000 deaths in South Africa in 2016 according to Statistics SA (2016). Statistics SA (2013 and 2011) stated that diabetes was the 4th largest cause of mortality in KwaZulu- Natal (KZN). In the year 2013, the IDF pointed out that South Africa was home to more than two and a half million diagnosed diabetics, and an approximate further million who were undiagnosed (IDF, 2013). Sahadew, Singaram and Brown (2016) established the distribution, incidence, crude prevalence, and prevalence of patients with DM in KZN and its districts during a 5-year period 2010 - 2014, as measured by the number of patients presenting at public health institutions. The projected diabetes prevalence rate of 34.1% in KZN, suggests that one in every three patients visiting a public health facility in the province is diabetic. This was factored into the estimated diabetes prevalence rates for KZN and the total diabetes prevalence rates for the districts. The estimated diabetes prevalence per district was as high as 43.5% in the district of uThungulu (Sahadew, Singaram and Brown, 2016).

4. Demographic stratification of Type 2 diabetes mellitus

Demographic factors such as age, gender, ethnicity, socio-economic status, and urbanization associated with nutrition transition and obesity are key contributors in the increased prevalence of diabetes (Pheiffer *et al.,* 2018).

4.1. Age

Populations are ageing worldwide, and the pace of the demographic transition is rapid in developing countries, including those in Africa (Werfalli *et al.,* 2018). The country with the largest ageing population in Africa is South Africa, with more than 1 in 6 individuals aged 50 years and older. An estimated 8% of the current population is aged 60 years and older equating to approximately 4.2 million people and is projected to increase (Pillay and Maharaj, 2013). According to the WHO (2015), T2DM is usually more frequent in older adults than younger people. Werfalli *et al*. (2018) conducted a cross-sectional study on 4037 South African adults aged 50 years and older. The total prevalence of self-reported diabetes was 9.2% (95% CI: 7.8,10.9), which increased with age: from 7.1% (95% CI: 5.4,9.2) amongst 50- to 59-year-olds, to 10.6% (95% CI: 8.0,14.0) amongst 60–69-year-olds, to 12.4% (95% CI: 9.1,16.7) amongst those 70 years and older (Werfalli *et al*., 2018). Similar results were obtained from a cross sectional study conducted in Ireland, with prevalence's are 55 to 64 years (6.50%), 65 to 69 years (10.75%) and 70 and above years (12.10%) (Sinnott *et al.,* 2017). This data demonstrates that prevalence increases with age and notable that diabetes is more prevalent among 70 years and older patients (Sinnott *et al*. 2017).

Limited global data exists on the prevalence and incidence of newly diagnosed T2DM in children and adolescents. Among the earliest reports of T2DM in children were those from the Pima Indians (Chandak *et al.,* 2017). The prevalence of T2DM in youth has increased over time in the Pima Indian population, for example, in girls aged 15 to 19 years, T2DM prevalence increased from 2.73% in 1967–1976 to 5.31% in 1987–1996, while, in boys, it increased from 2.43% to 3.78% over the same time periods (Chandak *et al.,* 2017).

Much less is known about T2DM in children in other populations because most studies have relied on clinical diagnoses rather than case finding by glucose tolerance testing. In India, small gestational age and nutritional deficiencies such as vitamin B12 deficiency, were associated with other diabetes risk factors (Chandak *et al.,* 2017). Increased T2DM incidence in children and young adults exposed to maternal T2DM in utero has been observed in Hispanic-Americans and other populations (Chandak *et al.,* 2017). Cross-sectional data on clinically diagnosed T2DM in different racial/ethnic groups were obtained in a youth study in South Africa (n>232) (Spanakis and Golden, 2013). The prevalence of T2DM was reported to be generally very low in children aged 0 to 9 years, regardless of race/ethnic group (Spanakis and Golden, 2013). The highest reported prevalence was observed among children and adolescents of Asian descent: 0.021 and 1.45 per 1000 people at 0 to 9 and 10 to 19 years of age, respectively (Spanakis and Golden, 2013). As the diabetes epidemic matures, the age at onset will shift to younger age-groups and early-onset T2DM will emerge (Mbanya *et al.,* 2010).

Peer *et al*. (2012) reported diabetes prevalence in Asian children and adolescents aged 10 to 19 years at 0.52 and 0.46 per 1000 people, respectively, while African children and adolescents have a very low prevalence of T2DM at age 10 to 19 years of 0.18 per 1000 people. During 2011 and 2012, 5300 children and adolescents aged between 10 and 19 years were diagnosed with T2DM, and the incidence rates were higher among South African youth. The literature, however, seems to have consensus on the argument that older people have a higher probability of prevalence of diabetes compared to younger groups (Peer *et al*., 2012).

4.2. Gender

The steep rise of T2DM and its associated complications correlates with gender differences (Kautzky-Willer, Harreiter, and Pacini, 2016). Gender differences are equally important in development, awareness, presentation, diagnosis, and therapy, as well as prevention of the lifestyle associated disease T2DM (Figure 3). Figure 3 illustrates how

the social conditions (upper) and biological factors (lower) influence the development of germ cells, fetal programming, the newborn, puberty, reproductive age, ageing, and especially the manifestation of T2DM in men and women as well as the progression of its complications and comorbidities.

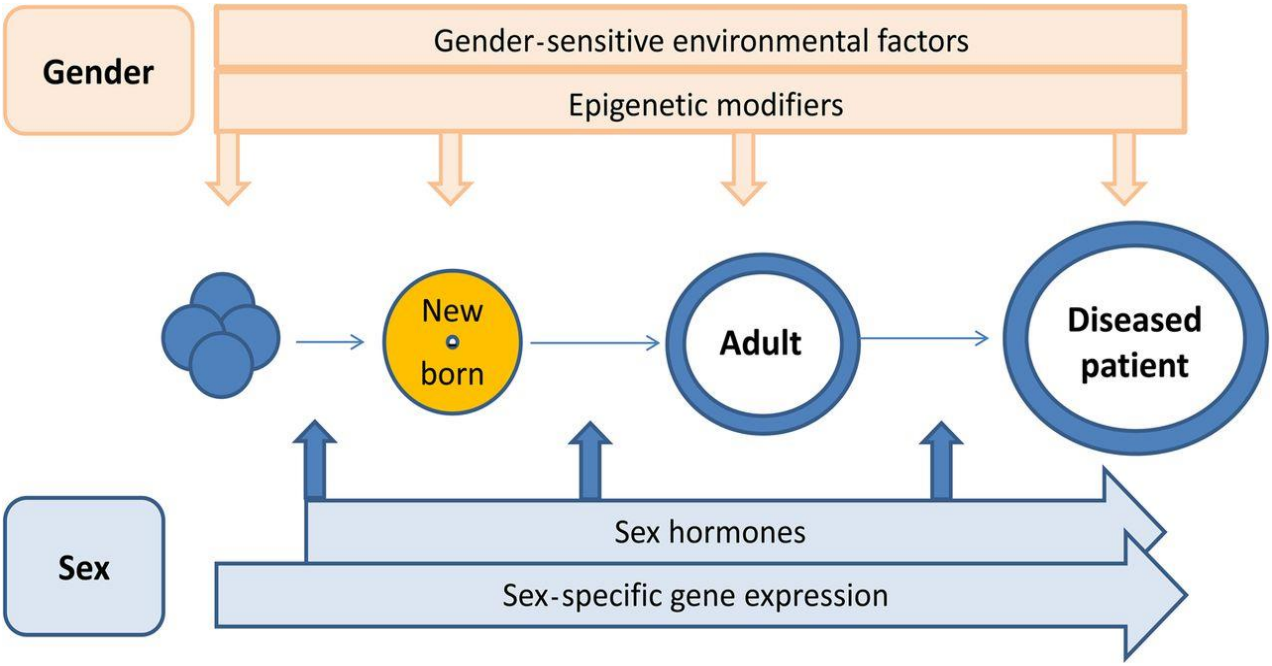

Figure 3: Lifelong impact and interaction between sex and gender on development and outcomes of T2DM (Source: Regitz-Zagrosek *et al.,* 2016)

Current literature suggests that DM disproportionately affects women (Peters and Woodward, 2018 and Kapur and Seshiah, 2017). A comparative study by Hanson, Rong and Kobes (2015) found that women with diabetes generally have poorer glycemic control and are less likely to reach the goals for hemoglobin A1c (HbA1c) compared with men (Hanson, Rong and Kobes, 2015). Several studies reported that the male sex is a risk factor for the development of T2DM (Chen, Magliano and Zimmet, 2012; Yang *et al.,* 2010, Tracey *et al*., 2016 and Wändell and Carllson, 2014). A cohort study in northern Sweden noted that the prevalence of T2DM was 14.6% in men and 9.1% in women

(p<0.001) (Nordström *et al*., 2016). The mean BMI was slightly higher in men than in women (27.3 vs 26.6 kg/m^2; p= 0.001), with a greater difference in mean visceral fat mass (1987 vs 1077 g; p<0.001). After adjustment for physical activity and smoking, men had approximately double the odds of having T2D compared with women (OR=1.95; 95% CI, 1.38–2.76) (Nordström *et al*., 2016). In addition, a comparative analysis by Chen, Corona and Sikora (2012) found that among women in the US, black American women with diabetes had a higher all-cause mortality (Chen, Corona and Sikora, 2012). Among men with diabetes, the mortality rate in cardiovascular disease had declined at a rate comparable with non-diabetic men over the past decades but there is still an almost three-fold increase due to diabetes (Chen, Corona and Sikora, 2012). However, Chandak *et al*. (2017) found disparities in the prevalence of diabetes amongst 174 participants comprising men and women. These disparities may be attributed to differences in physiology, treatment response, and psychological factors (Chandak *et al*., 2017). Sex differences in hormonal pathophysiology may also be critical factors in as far as data on sex differences in disease course and outcome is concerned (Chandak *et al.,* 2017).

Based on a systematic review, South African women were more predisposed to diabetes compared to men (Pheiffer *et al*., 2018). Major risk factors for the development of diabetes among women were obesity and poor diet (Pheiffer *et al.,* 2018). These epidemiological findings are supported by a South African longitudinal study (Peer *et al.,* 2012), who reported that men had increased insulin resistance and develop diabetes at a younger age and lower BMI than women. The data is indicative that the males' overall propensity for visceral and hepatic deposition of lipid is higher (Peer *et al*., 2012). In contrast, women were found to have more exposure to preferential subcutaneous lipid deposition. These male-female pattern adipose distributions, commonly referred to as pear- and apple-shaped obesity respectively, are regulated by sex hormones and apple/central adiposity is independently correlated with diabetes status irrespective of BMI or gender (Divoux *et al*., 2020).

4.3. Ethnicity

The global distribution of the diabetes prevalence is related to ethnicity (Cowie, Cassangrade and Geiss, 2018; Cheng, Reich and Haiman, 2012 and Spanakis and Golden, 2013). A study in the United Kingdom (UK) found that the socio-economic factors related to ethnicity were strongly correlated to the rise in diabetic cases (Lutsey *et al*., 2010). Prevalence was higher among white respondents compared to African immigrants from Africa living in the UK (Lutsey *et al*., 2010). Lutsey *et al.* (2010) also noted that among the African immigrants, age and socioeconomic status was a significant control factor, a reminder of the confluence of the variety of factors that influence the prevalence of diabetes. A cross-sectional multi-ethnicity study (n>200) in the US investigated the effect of BMI in predicting the prevalence of diabetes among different ethnicities and confirm a significant correlation between the two factors (Hanson, Rong and Kobes, 2015). The data indicate that the correlation was more significant amongst Chinese Americans ($p<0.0001$) whereas the lowest prevalence was recorded among black Americans ($p=0.41$). In contrast, Chen, Corona and Sikora (2013) confirm that ethnic variation in DM exist between African Americans and Caucasians (Chen, Corona and Sikora, 2013). Interestingly, their data suggest that this was not explained by the differences in the distribution of family income, education, marital status, alcohol history, physical activities, body mass index, age, and smoking history (Chen, Corona and Sikora, 2013).

A study was carried out among Chinese, Filipino, South Asian, Japanese, Korean, Vietnamese, Mexican, Hispanic, African American, Caucasian, and Native American adults (n= 46,091, projected n= 26.6 million) (Choi *et al.,* 2013). The highest age-adjusted diabetes prevalence was seen in Native Americans (32.4%), Filipinos (15.8%), and Japanese (11.8%) among men and in Native Americans (16.0%) and African Americans (13.3%) among women. Caucasian and Mexican men had higher diabetes prevalence than women (Choi *et al.,* 2013). A meta-analysis T2DM study conducted by Meeks *et al*. (2015) in various ethnic minority populations resident in Europe compared to their host European populations, indicate that South Asian had 3.7 (95 % CI 2.7–5.1) higher odds

ratio for T2DM compared to their European host populations (Meeks *et al*., 2015). On the contrary, Bangladesh demonstrates the highest odds ratio for T2DM, (6.2, 95 % CI 3.9–9.8), followed by Pakistanis (5.4, 95 % CI 3.2–9.3) and Indians (4.1, 95 % CI 3.0–5.7) compared with Europeans (Meeks *et al*., 2015).

Despite the large differences in DM incidence rates among different populations worldwide, the progression from high-risk overweight or obese states with impaired glucose regulation, to overt diabetes, occur at similar rates and respond similarly to preventive interventions amongst different racial/ethnic groups in the US (Chen, Corona and Sikora, 2012). Most behavioural or medical interventions for diabetes prevention showed positive result in racially/ethnically diverse populations (Lutsey *et al*., 2010). The effects of the similar interventions used in different racial/ethnic groups were not significantly different, for example, metformin and lifestyle interventions influenced the progression to T2DM proportionately (Spanakis and Golden, 2013). Despite the racial/ethnic differences in diabetes prevalence, current methods for diabetes prevention are the same across racial and ethnic categories.

People of African origin living in the United Kingdom have higher prevalence of diabetes than those living in African countries, whereas prevalence is intermediate in individuals of African ancestry living in Jamaica (Moltke *et al.,* 2014). A comparison between Indians living in the US and those living in urban India (Chennai), showed that India had higher prevalence of diabetes than the Indian Americans (Mahajan, Taliun and Thurner, 2018). In addition, the prevalence of diabetes in urban Ghana was much higher than in rural Ghana and comparable with that of African-origin populations in urban Europe (Moltke *et al.,* 2014). These studies implicate environmental factors associated with urbanisation as contributing to the high risk of diabetes in migrant populations. Peer *et al*. (2012) evaluated 129 participants and found that the annual age-adjusted incidence of diagnosed diabetes was higher in African individuals (9.0 per 1000 people) and individuals of Asian origin (8.4 per 1000 people) compared with other individuals (5.7 per

1000 people) in the population who are non-white (Peer *et al.,* 2012). Overall, the incidence of diabetes increased rapidly between 1990 to 2008, followed by a leveling off and then a decrease from 2008 to 2012; however, this primarily occurred in African individuals, while the incidence continued to rise in Asians and white individuals during this same time period (Peer *et al*., 2012).

5. Risk factors for Type 2 diabetes mellitus

Several risk factors for T2DM have been identified through systematic reviews and meta-analyses of observational studies (Bellou *et al*., 2018). Genetics, environmental, and metabolic risk factors play a critical role in the development of T2DM. People who have a strong family history of DM, older age, obesity, and inactivity are at the greatest risk of developing T2DM (Kyrou *et al.,* 2020).

5.1. Genetic predisposition

Type 2 diabetes mellitus is reported to be an inherited disease (Lyssenko and Laakso, 2013), and genetic factors determine how vulnerable an individual is to T2DM. Genetic risk factors for T2DM is supported by two major findings namely, ethnic differences in the prevalence of T2DM and a strong family history of T2DM (Kyrou *et al.,* 2020). The estimates for the heritability of DM range between 20% to 80%, and evidence for heritability originates from various population, family, and twin-based studies (Hipp and Chalise (2015). The lifetime risk of developing diabetes was 40% for individuals who have one parent with diabetes and 70% if both parents are affected (Hipp and Chalise, 2015). First-degree relatives of individuals with diabetes are about 3 times more likely to develop the disease than individuals without a positive family history of the disease. The concordance rate in monozygotic twins is approximately 70% whereas, the concordance in dizygotic twins has been observed to be only 20% to 30% (Sahu and Prasuna, 2016). A significant proportion of this heritability reflects heritability of obesity rather than

diabetes, obesity being a major driver of diabetes in every population (Hipp and Chalise, 2015; Strate *et al.,* 2013; Willemsen *et al*., 2015 and Ali, 2013).

Moreover, T2DM is twice as prevalent among African Americans as it is among European Americans (Cheng *et al*., 2012). African Americans are twice as likely as whites to develop incident T2DM which is a disparity that persists even after extensive adjustment for socioeconomic status (SES) and behavioral risk factors. Based on this disparity, it is possible that genetic factors affect ethnic susceptibility to T2DM (Cheng *et al.,* 2012). Among diabetic patients, African ancestry was 1.6% more prevalent than among non-diabetics ($p<0.001$, adjusted for study) (Cheng *et al.,* 2012). The odd ratios (ORs) for diabetes were higher with increasing tertiles of African ancestry (p for trend<0.001,) after adjustment for age, sex, and study. In the US, African Americans have one of the highest prevalence of T2DM (Ng, 2015), however, little is known about their genetic risks. The association between genetics and T2DM was evaluated, and the findings show that the African American population consist of 80 % African and 20 % European ancestry (Cheng *et al.,* 2012). However, given the higher prevalence of T2DM in African Americans than in Europeans, some disease-associated genetic variants may differ considerably between African American ancestral populations and contribute to the disparity in disease prevalence. In contrast, Ramya *et al*. (2013) investigated the genetic association of eight variants of the adiponectin gene of T2DM in a south Indian population and found that the adiponectin gene variants contribute to the genetic risk towards the development of T2DM (Ramya *et al*., 2013). Vilvanathan *et al*. (2014) indicated that India ranks second in the world in terms of diabetes prevalence, just after China. A study was carried out among the Asian Indian population from Hyderabad, India to determine the association between T2DM and candidate genes (Khan *et al.,* 2015). The data suggests that family history was not significantly associated with T2DM ($p>0.05$), although family history was closely associated with T2DM (58.4%), showing an independent association (Khan *et al*., 2015). Yako *et al.* (2016) reported that T2DM is spreading faster in Africa than any other continent, driven by the dual effects of genetic and environmental factors. Based on the data emanating from a systematic review and meta-analyses on genetic markers of T2DM

in African populations, most genetic markers originate from North African countries. The markers are scarce and insufficient to reliably inform the genetic architecture of T2DM across Africa.

In a South African study, the familial clustering of diabetes risk found in various family studies are not entirely due to genetic factors (Mbanya *et al*., 2010). Epigenetic processes can produce inherited risk over one or several generations, intrauterine and pregnancy related factors can impact the risk of siblings, and shared environment can be hard to control for in many such studies (Mbanya *et al*., 2010). Thus, the genetic component of diabetes may turn out to be less than what was estimated in older studies. Candidate gene studies and linkage analysis identified a few diabetes risk genes, but their overall contribution to the observed heritability of diabetes remained small and it was clear that other techniques were needed to look for variants that were not easily identified by these methods (Mbanya *et al*., 2010).

5.2. Lifestyle and behavior

Risk factors of diabetes can be categorized as metabolic or physiological risk factors such as obesity, and hyperlipidemia which is high levels of fat in the blood and 'modifiable behavioral risk factors namely unhealthy diet, physical inactivity and the harmful use of tobacco and alcohol (Polonsky, 2012; Hu, 2011 and Barik *et al.,* 2016). Diabetes risk factors target various organs of the body, but these are connected by endocrine, metabolic, immune, and neurological networks (Figure 4). Since the loss of insulin production is the ultimate cause of developing overt T2DM, environmental and lifestyle factors is likely to cause β-cell damage directly or indirectly (Kaneto, 2015; Brun and Maechler, 2016 and Ertunc and Hotamisligil, 2016). The recognition of the environmental changes and lifestyle factors responsible in theory may contribute to more effective management to decrease the number of new cases to reach those of 20–40 years earlier (Kolb and Martin, 2017).

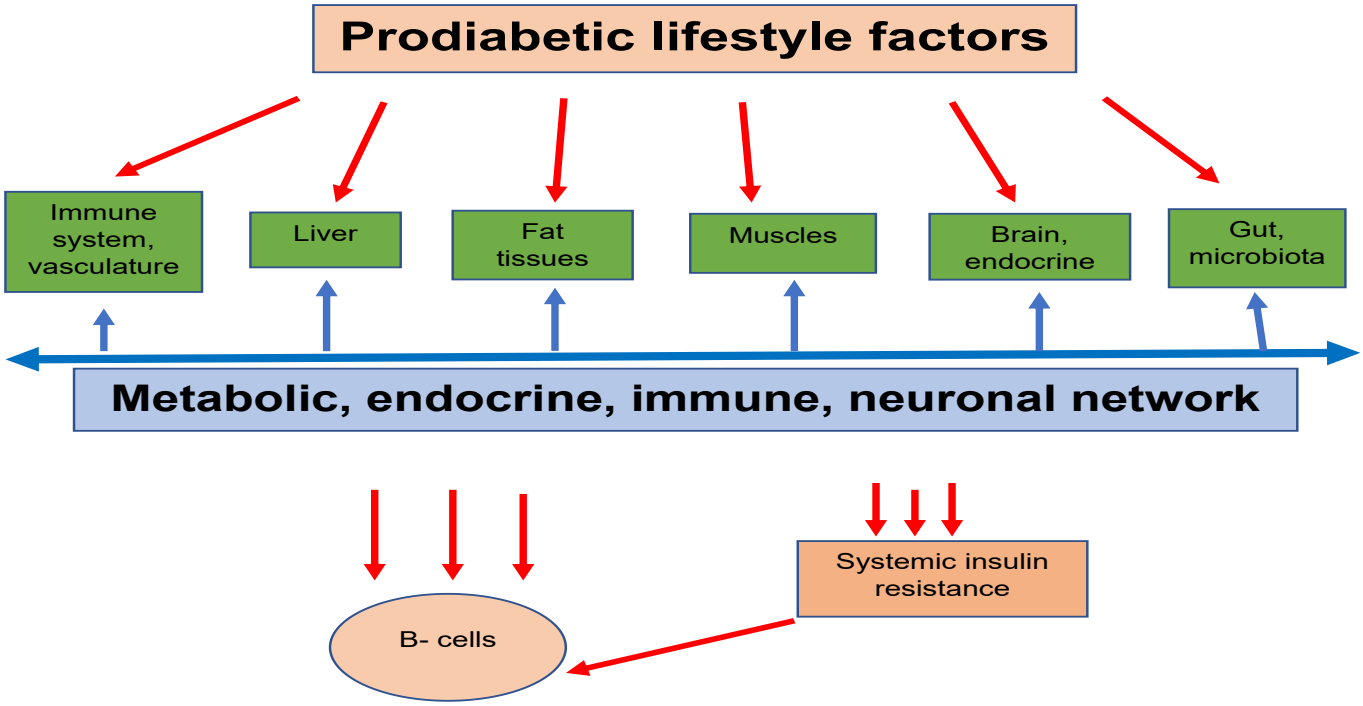

Figure 4: Prediabetic lifestyle factors target regulatory networks (Source: Kolb and Martin, 2017)

A cross-sectional study reports that in Indian and other populations in which vegetarianism is common, vitamin B12 deficiency is highly prevalent (Mahajan, Taliun and Thurner, 2018). Maternal vitamin B12 deficiency and hyperhomocysteinaemia are related to poor fetal growth, and subsequent insulin resistance and adiposity in childhood (Mahajan, Taliun and Thurner, 2018). High folate status worsens the situation, indicative of a balance between vitamin B12 and folate is essential. Moreover, Indian diets are associated with macronutrient imbalances; they tend to be high in energy and carbohydrates and have a high glycaemic index (Ebrahim, 2010). Additionally, South Asians appear to be less physically active than their European counterparts, suggestive that this may contribute to their higher and premature susceptibility to T2DM (Mahajan, Taliun and Thurner, 2018). Physical activity is reported to lower blood pressure and confer protectiveness against the development of DM (Stanford and Goodyear, 2014). Exercise

enhances expression of the genes that regulate insulin receptors, thus enhancing plasma glucose reuptake, and normalizing glycemic index (Stanford and Goodyear, 2014).

A descriptive study in the US consisting of 266 participants, demonstrated a strong association between DM prevalence with current smoking, alcohol, physical activity, body mass index, and age (Ng *et al.,* 2020). Smoking results in the vasoconstriction, thus increasing peripheral resistance, and elevating the blood pressure, thus supporting its role in DM development given the nexus between DM and hypertension (Centers for Disease Control and Prevention, 2010). Elevated BMI is associated with DM due to the extra load placed on the myocardium as result of increased cardiac contractibility (Ashraf and Baweja, 2013). This leads to increased heart rate and stroke volume, consequently elevating the cardiac output and blood pressure (Ashraf and Baweja, 2013). Similarly, the nexus between hypertension and elevated blood glucose level may explain the observed relationship between BMI and glucose intolerance. A direct association between weight and DM is insulin insensitivity observed among overweight individuals (Al-Goblan, Al-Alfi and Khan, 2014).

Driven by rapid globalization and urbanization with subsequent changes in diet and the adoption of a sedentary lifestyle, a case study in Zimbabwe led by Chandak *et al*. (2017) reported an expansion in the diabetes epidemic in line with global increases in overweight and obesity (Chandak *et al*., 2017). Being overweight significantly increases the risk of diabetes (Leitner *et al*., 2017). A meta-analysis of Kenyan populations by Kengne *et al.* (2013), described overweight/obesity as a major but modifiable risk factor for diabetes. Another Nigerian meta-analysis steered by Agyemang *et al.* (2016), found that abdominal obesity was positively associated with increased probability of metabolic syndrome. Across many sub-Saharan African countries, obesity is linked to both urban residence and wealth, i.e. the more wealthy a person is, the more likely he or she will be overweight or obese due to nutritional transition (Agyemang *et al*., 2016). While the prevalence of obesity is mostly among women in West Africa, South Africa, and Tanzania,

approximately 61% of the South African population are reported to be overweight and/or obese (Kengne *et al*., 2013). Moreover, a complex set of cultural, psychosocial, and biological factors influences the maintenance of healthy weight, and these factors affects diet, physical activity and ultimately obesity prevalence, and consequent increase in diabetes onset (Ford, Patel and Narayan, 2017)

6. Co-morbidities of type 2 diabetes mellitus

Type 2 diabetes mellitus is one of the leading causes of premature morbidity and mortality worldwide, resulting in microvascular and macrovascular complications related with this disease (Pratley, 2013 and Chawla *et al.,* 2016). Various studies report that a number of people with newly diagnosed T2DM are already affected by chronic complications (Winkley *et al*., 2013; Kostev *et al*., 2014; Christensen *et al*., 2018 and Zaharia *et al.,* 2019). According to Schram *et al.* (2014), current in-depth knowledge is urgently needed in order to avoid the development of classic complications and the emerging comorbidities of T2D. In developed countries, T2DM increases risk of cardiovascular disease (CVD) two-fold and is the leading cause of blindness, and responsible for approximately 40 % of the last stage of renal failure and over 60 % of non-traumatic lower-limb amputations (Sarwar *et al*., 2010 and Ravona-Springer *et al.*, 2010). On the other hand, mortality as a result of these emerging comorbidities is about 70 % greater in people with T2DM as compared to individuals without diabetes (Schram *et al.*, 2014).

The WHO (2011) reports that diabetic retinopathy is the main cause of blindness among people between 20-to-74-year-old, whereas diabetic nephropathy is the leading cause of chronic kidney disease which affects an estimated 40% of T2DM patients (WHO, 2011). More than 80% of nontraumatic limb amputations result in a foot ulcer or injury thus making the risk of amputations in individuals with diabetes up to 25 times more likely (Pratley, 2013). A survey-based study was carried out among 40 diabetic patients by Sivakumar (2015) which aimed at delineating the most commonly associated diseases or co-morbidities associated with diabetes and to stratify the associated diseases and co-

morbidities between men and women. In this sample size of 40, diabetes was more prevalent in men (60%) than women (40%). Additional conditions and symptoms were subdivided into groups such as oral disorders, cardiac and respiratory maladies, neuropathy, muscular and joint related disorders, and other miscellaneous problems. For oral disorders, dry mouth (53%), tooth decay and infection (45%) and loosening of teeth (38%) were identified as the key experiences; for cardiac and respiratory problems, chest pains and shortness of breath was experienced and had an equal distribution of 35%; followed by high blood pressure, vision difficulty, arthritis/ joint pain and numbness of hands and feet, with a percentage of 63, 60 and 45 respectively. Other miscellaneous issues experienced included slow wound healing (45%), fatigue (38%) and hypoglycemic attacks (38%); followed less frequently by congestion, Haemorrhoids, and weight gain. The data from this study indicates that diabetes is not a singular condition, instead it is a spectrum of various other comorbidities, which have to be identified and treated correctly (Sivakumar, 2015).

Notably, hypertension occurs in more than 50% of patients with DM and adds significantly to both micro- and macro-vascular disease in diabetes (Lastra *et al.,* 2015). A meta-analysis of 102 prospective studies comprising of 698782 individuals highlights that DM potentially doubles the risk for coronary heart disease, stroke and deaths from heart failure, cardiac arrhythmia, sudden death, hypertensive disease, and aortic aneurysms (Sarwar, 2010). These data suggest that about 10% of vascular deaths in industrialized countries can be attributed to diabetes, and this burden will rapidly rise as the incidence of diabetes continues to rise (Sarwar, 2010). The increased prevalence of risk factors such as hypertension, dyslipidaemia and obesity in these patients are related to this risk. However, the improved CVD in T2DM patients cannot be solely attributed to the higher prevalence of traditional risk factors, therefore other non-traditional risk factors are important and must be considered in people with T2DM (Martín-Timón *et al*., 2014). Prior to the onset of diabetes, many patients already show metabolic abnormalities, such as dyslipidemia, further contributing to the development of complications (American Diabetes Association, 2010). The most important outcomes of T2DM are chronic

complication which diminishes the quality of life, becomes of its burden on the health care system and the rise to diabetic mortality (Liu *et al.,* 2010). Globally, diabetic retinopathy, has become a major cause of blindness, and clinical epidemiologic studies suggest that foot ulcers precede more than 85% of non-traumatic lower extremity amputations in diabetic individuals (Solli, Stavem and Kristiansen, 2010).

There is substantial epidemiological evidence that supports the relationship between T2DM and associated comorbidities (Iglay *et al.,* 2016; Adriaanse *et al.,* 2016; Nowakowska *et al.,* 2019; Xu, 2016). A cross-sectional Chinese hospital-based study reported that while 1524 (48.0%) T2DM patients had no recognizable complications, 792 (52.0%) were affected by at least one diagnosed chronic complication (Liu *et al*., 2010). The prevalence of cardiovascular and cerebrovascular complications, neuropathy, nephropathy, ocular lesions, and diabetic foot disease was 30.1%, 6.8%, 17.8%, 10.7%, 14.8% and 0.8%, respectively. The most frequent cardiovascular condition was angina (14.2%) (Liu *et al*., 2010). Approximately, 225 subjects suffered from ocular complications, with the most prominent conditions being cataract (9.8%) and retinopathy (6.1%), whereas foot complications were observed in 12 patients (Liu *et al*., 2010). Female patients had a significantly higher prevalence of complications than male patients ($\chi 2 = 9.75$, $p=0.002$). Approximately 50% of the participants in this cohort that was newly diagnosed with T2DM, reported target organ/ system damage. Secondly, microvascular complications (eye, kidney, nerves) and neuropathy abnormalities were more common than those documenting retinopathy or nephropathy (Liu *et al*., 2010).

A recent cross-sectional survey was carried out among 912 T2DM patients who attended different urban primary health care facilities at Bhubaneswar, India report that the second largest diabetic population in the world is found in India (Pati and Schellevis, 2017). Their results indicate that 84% patients had one or more than one comorbid condition (Pati and Schellevis, 2017). Hypertension (62%), acid peptic disease (28%), chronic back ache (22%) and osteoarthritis (21%) were there most common comorbidities experienced. The number of comorbid conditions was greater amongst males (0–14) than females (0–6).

Moreover, the above 60-year-old age group showed the highest number of comorbidities. Male patients below 40 years of age presented with either single (53%) or three comorbidities (11%) whereas among female patients of the same age group single (40%) or two comorbidities (22%). Hence, age was a strong independent predictor for diabetes comorbidity (Pati and Schellevis, 2017). In contrast, a retrospective study conducted in General Hospital Ughelli Delta State, Nigeria, amongst 53421 participants, confirm that 19391 (36.29%) were females, 18559 (34.75%) males and 15435 (28.95%) children. The overall prevalence of diabetes within this cohort was 25.46% with the prevalence among males 46.63% and females 53.37% respectively (p=0.000). The most frequent complications experienced was kidney failure (27.87%) and heart attack (27.27%), followed by erectile dysfunctions (21.0%) and CVD (10.0%) (Agofure, Okandeji-Barry and Ogbon, 2020). Diabetes comorbidities that were prevalent included hypertension (54.0%), peptic ulcer (7.0%) and asthma (4.0%) (Agofure, Okandeji-Barry and Ogbon, 2020). A cross-sectional household survey consisting of 25532 people in South Africa confirm that only 1000 respondents (5%) reported having diabetes. Of this 1000, approximately 73% had at least one of the CVD chronic illnesses, whilst 27% reported having diabetes and no CVD chronic illness (Mutyambizi *et al*., 2017). An estimated 2% of diabetic respondents presented with three CVD chronic conditions such as stroke, heart disease and high blood pressure which were more prevalent amongst diabetic individuals compared to non-diabetics (Mutyambizi *et al.,* 2017).

In South Africa, a study was conducted at six randomly selected intervention clinics and six control primary health care clinics in the Tshwane district in a cluster randomized clinical trial. Overall, a total of 599 patients were enrolled in the study from 12 primary health care clinics (328 from the intervention clinics and 273 from the control clinics). Eighty seven percent of patients had normal vision, however, 4.5% of patients were blind. Retinopathy was found in 29% of patients as well as subjective neuropathy which was present in more than 97% of patients. Chronic kidney disease was observed in 7.4% (N=24) of patients based on the glomerular filtration rate calculation. Macrovascular complications were noted in 43% of patients suffering from dyspnoea and 0.6% from

angina; 17% possibly had a previous myocardial infarction; and 1.3% suffered from intermittent claudication (Webb, Rheeder and Van Zyl, 2015). Erectile dysfunction was reported by 88% of diabetic men, of which, 36% of the cases were severe. Furthermore, Werfalli *et al.* (2018) conducted a cross-sectional study amongst 4037 South African adults aged 50 years and older, of which, 3836 (90.9%) were 50 years and older. The study found convincing evidence of lower quality of life in participants with diabetes (−4.2, 95% CI: −9.2,0.9; p-value< 0.001). Results obtained also indicated that diabetes was associated with a higher disability rate (multiplicative effect: 2.1; 95% CI: 1.59,2.9; p-value:<0.001). A notable fact is that unlike the above findings or other studies conducted by Väätäinen *et al.* (2016); Bourdel-Marchasson *et al.* (2013) and Suzman (2010), age and gender were not associated with a high level of disability. Appropriate health care for older adults with diabetes can reduce or eliminate disability and avoid diminished quality of life associated with poor diabetes management which leads in disabling complications such as stroke, kidney disease, amputations, and impaired vision (Werfalli *et al.,* 2018).

7. Management of type 2 diabetes mellitus

7.1. Complementary and alternative medication

Complementary and alternative medicine (CAM) refers to a series of medical and health care practices and products that are not a part of conventional medicine. However, inconclusive evidence remains on the safety and effectiveness of CAM when compared to conventional medicine (Su and Li, 2011). There is a developing trend for patients to use complementary and alternative medications (CAM) in an attempt to improve or eliminate the negative outcomes of their illnesses and improve their general wellbeing. Moreover, CAMs have gained academic, industrial, and economic interest due to its increased usage (Medagama and Bandara, 2014; and Sheikhrabori *et al.,* 2016). Complementary medicine is used with conventional therapy (Medagama and Bandara, 2014), whereas alternative medicine is used instead of conventional medicine (Medagama and Bandara, 2014). Estimates shows that over 80% of people living in developing countries still depend on CAM for treatment health conditions (Ranasinghe *et*

al., 2012). Several types of complementary medication are used including yoga, acupuncture, massage therapy, aromatherapy, and traditional indigenous medicinal herbs (Pandey *et al*., 2011). The mechanism of some of the commonly used CAM for lowering the blood glucose is shown in Table 1.

Table 1: Complementary and alternative therapy (CAT) with mechanism for lowering blood glucose (Pandey *et al*., 2011).

CAT	**MECHANISM**
Yoga	Improve in insulin sensitivity and decline in insulin resistance.
Massage	At an injection site increase serum insulin, thereby decrease blood glucose.
Acupuncture	Act on pancreas to enhance insulin synthesis, accelerate the utilization glucose, resulting in blood sugar.
Aromatherapy	Ameliorate the stress of coping with a lifelong chronic condition such as diabetes.
Momordica charantia	Not known (in diabetic rabbit models it possesses a direct action similar to insulin).
Trigonella foenum graceum	Hypoglycemic effect may be mediated through stimulating insulin synthesis and/or secretion from the beta pancreatic cells of Langerhans.
Gymnema sylvestre	This is attributed to the ability of gymnemic acids to delay the glucose absorption in the blood.
Azadirachta indica	Not known
L-carnitine	Effect insulin sensitivity and enhance glucose uptake and storage.
Vanaduim	Insulin mimetic with up gradation of insulin receptors.
Chromium	Facilitates insulin binding and subsequent uptake of glucose into cell.
Vitamin E	Potent lipophilic antioxidant activity with possible influences on protein glycation lipid oxidation and insulin sensitivity and secretion.

A cross sectional study consisting of 240 diabetic patients demonstrated a 62.5% prevalence of CAM use (Ching *et al.,* 2013). Females were also 1.8 times more likely than male to use CAM, whilst frequents CAM users were approximately 75% of Malays, 18% of Indians and 6% of Chinese people. Biological therapy (50.0%) was the most widely used treatment, followed by manipulative-body based systems (9.2%), energy system (8.8%), alternative medicine systems (4.6%) and mind-body system (1.7%) (Ching *et al.,* 2013). Similarly, in a retrospective Taiwanese cross-sectional survey, participants reported an extensive use of CAM with conventional medicines (Chang, Wallis and Tiralongo, 2010). The prevalence of CAM use was 22.7% before and 61.0% after diagnosis with T2DM with nutritional supplements being the most commonly used CAM before and after diagnosis (Chang, Wallis and Tiralongo, 2010). The CAM modalities demonstrating an increase in the number of people using them after diagnosis were nutritional supplements, Chinese herbal medicines, diet modifications, manipulative-based therapies, biofield therapy, bioelectromagnetic-based therapies, supernatural healing therapies, and mind-body therapies (Chang, Wallis and Tiralongo, 2010). In contrast, the proportion of people using acupuncture, cupping and scraping, and aromatherapy remained the same before and after diagnosis (Chang, Wallis and Tiralongo, 2010). Raja *et al.* (2019) carried out a study at a tertiary care hospital in Pakistan and reported a 57.8% (n=151) use of CAM therapies. The most frequently used CAM practice was herbs (n=121; 80.1%), specific diets (n = 98; 64.9%), followed by cupping (n = 68; 45.0%). A significant association was observed between CAM practices and diabetes-related complications ($p<0.000$), poor glycemic control ($p<0.000$), lack of trust in pharmaceutical products ($p<0.000$), poor patient-doctor relationship ($p=0.06$), CAM products being readily available and cheaper ($p<0.000$) and belief that CAM products have fewer side effects ($p<0.000$) and can help in diabetes control ($p<0.000$). Thus, the use of complementary medicine products among Pakistani diabetic population is reportedly high.

7.2. Alternative/ traditional medicine/ home remedies stratified by Indian and African population

7.2.1. **Indian Ayurveda or herbal medicine**

Traditional medicine (TM) use is recognized as a popular means of treatment amongst those diagnosed with DM (Chege *et al.,* 2015). People living in developing countries depend greatly on TM for their health care needs (Frimpong and Nlooto, 2018). Almost 40% of those residing in the US use TM, in contrast to the reported 52.79% South Africans (Frimpong and Nlooto, 2018). According to the WHO (2017), TM refers to the knowledge, skills and practices based on the theories, beliefs, and experiences indigenous to different cultures and used in the maintenance of health and is referred to as alternative or complementary medicine (TCAM) in many countries (WHO, 2017).

The use of Ayurveda medicine for T2DM, has shown marked improvement on patient outcomes in numerous case reports (Gordon, Buch and Baute, 2019 and Sridharan *et al.*, 2011). In SSA, TCAM usage is widespread, with many relying on it to maintain their health or prevent and treat communicable and NCD's (WHO, 2014). The economic influence of TCAM is extensive, contributing at least 2.9 billion rand to the South African economy alone (Mander, Ntuli and Diederichs, 2007). The results of a cross-sectional study conducted in Malaysia among 240 DM patients indicated that the prevalence of TCAM use was 62.5 % in which females were 1.8 times more likely than males to use TCAM (Ching *et al.,* 2013). Similar results were obtained from a Bahrain study conducted in 402 DM patients, in which 63 % used TCAM, of which females were the more frequent users (Khalaf and Whitford, 2010). In contrast, 80% of South Africans in the Eastern Province is reliant on TM as their primary source of health care (Keter and Mutiso, 2012). Several studies indicate that the main reasons for using TM include the reduced side effects, its cost-effectiveness, accessibility, and acceptability which assist in better controlling of diabetes and its associated complications (Ching *et al*., 2013; Chang, Wallis and Tiralongo, 2011 and Ahwinahwi and Chukwudi, 2016).

A cross- sectional study aimed at measuring the frequency and pattern of CAM utilization in people with diabetes was conducted amongst 263 patients in Nigeria (Ogbera *et al.,* 2011). Biodata, duration of diabetes, type and pattern of CAM utilization and adherence to prescribed medications were documented. The mean age of the 263 patients was 60 (10.7) years and the age ranged between 28 to 80 years. The findings demonstrate a prevalence rate of 46% CAM usage and the female to male ratio was 2:1. The main form of CAM usage included bitter leaf (Vernonia amygdalina), aloe vera, garlic, ginger, and local herbs. Adherence to prescribed medications was observed by 94% of respondents. The study concluded that CAM usage is an important facet of management of diabetes among patients with biological based therapies being the prevalent forms of CAM utilized, however, more assessments must be carried out to evaluate the impact of CAM on glycaemia (Ogbera *et al*., 2011).However, Medagama and Bandara (2014) observed conflicting data, when evaluating available literature pertaining to the role of Cinnamon, Bitter gourd (Momordica charantia) and Fenugreek (Trigonella foenum-graecum) for the treatment of diabetes. Worldwide, cinnamon is widely used as a flavoring agent in the food and beverage industry and most importantly, for its medicinal properties. Currently, cinnamon is sold as both a preventative and therapeutic supplement for the metabolic syndrome, insulin resistance, T2DM, hyperlipidaemia and arthritis (Rafehi, Ververis and Karagiannis, 2012). Data from a systematic review done to determine an association between cinnamon and diabetes, show that significant reductions in fasting plasma glucose levels and/ or glycosylated haemoglobin was noted in 5 of 6 studies included in the analyses (Akilen *et al*., 2012). Notably, the trial that failed to demonstrate a significant decline in HbA1C had a mean baseline value close to 7%, (range of 6.8% to 7.1%), in contrast to the HbA1C baseline values of 8.28% (Crawford, 2009) and 8.55% (Akilen *et al*., 2012) respectively. It is possible that the effect of cinnamon is minimal when glucose control is closer to normal, and it may exert a significant effect in reducing glucose as the values rise (Medagama and Bandara, 2014). On the other hand, of the 3 studies that reviewed the effectiveness of bitter gourd as a glucose lowering option, only one showed a reduction in fructosamine levels without a significant lowering of fasting plasma glucose (FPG) or postprandial glucose (PPG) (Fuangchan *et al.,* 2011); whereas 2 of them failed to show a significant lowering of blood glucose (Selvakumar *et al.,* 2017 and Efird *et al.,*

2014). Fenugreek seeds is widely used as a spice as well as a medicine (Medagama and Bandara, 2014). The leaves, chemical extracts and shoots of the plant have demonstrated antioxidant, anti-diabetic and hypocholesterolaemic properties. It also shares many of its glucose lowering mechanisms with cinnamon and stimulates the tyrosine phosphorylation of the insulin receptor and enhances glucose uptake into cells (Medagama and Bandara, 2014). However, these results require further evaluation in long-term clinical trials (Medagama and Bandara, 2014).

A Nigerian study conducted among 450 participants reported that despite the increased drive towards the use of TCAM, over 50% of those who participated indicated they do not prefer TCAM to western medicines (Ahwinahwi and Chukwudi, 2016). Contributing factors included the lack of scientific evidence, its low effectiveness, the lack of appropriate dosages, the risk of side effects, unreliability, difficulty in preparation and insufficient knowledge surrounding its use (Ahwinahwi and Chukwudi, 2016). Another study conducted in a Dubai population report a rise in the use of TCAM as a mode of diabetes management (Alalami, Saeed and Khan, 2017). However, this rise was accompanied by serious health complications when TCAM was used with conventional medical treatments, or when conventional treatments were completely abandoned in favor of TCAM (Alalami. Saeed and Khan, 2017).

7.2.2. **African traditional medicine**

African traditional medicine (ATM) frequently used by African populations, for the treatment of diseases prior to the advent of orthodox medicine, continues to overcome a portion of the healthcare burden for most of this population. Moreover, ATM is one of the oldest and most diverse of all medicine systems, even though the medicine systems are not efficiently recorded (Mothibe and Sibanda, 2019). African traditional healing is interwoven with cultural practices and religious beliefs and is therefore regarded as being holistic, involving both the body and the mind (Mothibe and Sibanda, 2019). It is estimated that approximately 72% of the Black African population use ATM (Mothibe and Sibanda,

2019). Over the past few years, South African ethnobotanical studies have explored the biological and pharmacological effects of several plants, viz., Aloe Ferox, Artemisia afra and Leonotis leonuris (Davids, Gibson and Johnson, 2016; Braünlich *et al.,* 2018 and Basson, 2017). These medicinal plants are primarily used as by communities mainly for DM, hypertension, and HIV infection (Mothibe and Sibanda, 2019). These plants form part of the list of potent medicinal plants with potential to be developed into commercial products (Odeyemi and Bradley, 2018 and De Wet, Ramulondi and Ngcobo, 2016).

However, due to the inherent side effects such as hypoglycemia, weight increase, gastrointestinal (GIT) disturbances, nausea, and diarrhoea of common oral hypoglycemic synthetic drugs like sulphonylureas biguanides metformin, and glucosidase inhibitors like Acarbose, researchers are now intensifying efforts in alternative and complementary medicines to assist in managing the burden of this epidemic (Hanewinckel, 2010). This is partly because herbal remedies are more efficient and have little or no adverse effects and could also be due to the fact that they form a vital component of the health care delivery system in most African nations (Hanewinckel, 2010). An earlier technical report indicated that 4 out of 5 citizens in African countries rely on folk medicines particularly herbal remedies for their primary health care requirements (Agyemang *et al.,* 2016). This could be ascribed to the efficacy and availabilities of these plants because they account for 25% of higher plants in the world comprising 5 400 with more than 16 300 medicinal uses (Agyemang *et al.,* 2016). South Africa accounts for 9% (approximately 30 000 species) of higher plants in the world, hence it is not surprising that over 3 500 species of these plants are used by over 20 000 indigenous healers (Lawson, 2013). Interestingly, about 80% of South Africans use plants for therapeutic purposes mainly because the cost of buying orthodox medicine or conventional treatment continues to increase (Balogun, Tshabalala and Ashafa, 2016 and Mahomoodally, 2013).

Based on the literature reviewed by James *et al.* (2018), biological-based therapies such as herbal therapy are the most common TCAM used in Sub-Saharan Africa, followed by

faith-based healing methods (prayer/spirituality) and mind-body therapies such as massage, traditional bone setting relaxation, mediation, and yoga (James *et al*., 2018). Herbal drugs with anti-diabetic activity are known for their therapeutic potentials within the traditional healthcare system, but despite their pronounced folkloric activity, they have not been commercially formulated as modern medicines (Ozioma and Chinwe, 2019 and Balogun, Tshabalala and Ashafa, 2016). This is despite the fact that their therapeutic properties serve as a potential source of hypoglycemic drugs and many of the compounds derived from these plants are used in diabetes management. This was confirmed by an ethnobotanical survey conducted on medicinal herbs employed in the control of diabetes from divergent regions, communities, and tribes within the African subregion (Hall *et al*., 2011).

The Basotho tribes are the largest population of blacks living in the Free State, Gauteng, and Eastern Cape provinces within South Africa (Balogun, Tshabalala and Ashafa, 2016). Hence, it is worth mentioning that their knowledge and usage of numerous medicinal plants in the treatment of various disorders such as diabetes and hypertension cannot be overemphasized (Balogun, Tshabalala and Ashafa, 2016). Vasudevan and Buch (2016) in the past conducted an ethnobotanical overview of plants utilized for diabetes control by the Basotho people and identified twenty-three (23) plants with such potentials. Sridharan *et al.* (2011) conducted a comprehensive review of these plants with a view to averting the possible extinction of these plants. This review was also intended to serve as a guide for possible future research on the scientifically unproven plants. Hypoxis hemerocallidea formerly referred to as H. rooperi (African potato) according to Hanewickel (2010) belongs to the *Hypoxidaceae* (star lily) family. The locally called star flower and yellow star (Eng.); sterblom and gifbol (Afr.); moli kharatsa and Lotsane (South Sotho); or Inkomfe (Zulu) is widely distributed in all provinces in South Africa, and in other African countries such as Botswana, Lesotho, and Swaziland (Hanewickel, 2010). There are over 76 species of the genus *Hypoxis* in Africa, 40 of which are found in South Africa while 16 others are endemic to South Africa (Balogun, Tshabalala and Ashafa, 2016). Traditionally, various parts of the plant are used in the treatment of various diseases such

as dizziness, burns, wounds, anxiety, depression or insanity, DM, cancer, polyarthritis, hypertension, and asthma (Mbanya *et al.,* 2010).

Previous studies reported that 80% of people residing in developing countries depend on TM as the primary remedy for various ailments such as CVD, DM, and hypertension (Sridharan *et al.,* 2011 and Peer *et al.,* 2012). Plant-based TMs are the most commonly used in primary health care in many developing countries such as Tanzania, where the majority of the population depends on TMs for the management of diabetes (Balogun, Tshabalala and Ashafa, 2016). A case study conducted by Vasudevan and Buch (2016) with 212 participants, corroborates this, confirming that 77% of diabetic patients in Northern Tanzania use TM. Their findings also suggest that various TM used by diabetic patients in Northern Tanzania, are undocumented, and hence their pharmacological properties with respect to blood glucose control have not been investigated. Thus, TM use may be attributable to sociocultural perspectives within the community and may contribute to disease-related complications. Most TM are common foods which include vegetables, flowers, fruits, seeds, spices, and herbs (Peer *et al*., 2012 and Chandak *et al.,* 2017).

8. The association between Coronavirus and type 2 diabetes mellitus

The Coronavirus disease (COVID-19), which is caused by a severe acute respiratory illness syndrome coronavirus 2 (SARS-CoV-2), has infected more than one hundred million individuals and resulted in approximately two million deaths to date. One of the most prevalent chronic complications worldwide is DM which significantly increases the risk of hospitalization and death among COVID-19 patients (Corrao *et al*., 2021). COVID-19 severity and mortality appeared to be independently related to DM and hyperglycaemia levels among Italians (Spagnolo, Manson and Joffe 2020, Holman *et al*., 2020; Grasselli *et al*., 2020 and Zhu *et al*., 2020). On the contrary, Hartmann-Boyce *et al.* (2020) indicated that there is limited data available on the association between blood glucose control and COVID-19 outcomes to date. However, Bode *et al.* (2020) conducted

a retrospective study among 451 COVID-19 patients with diabetes and/or hyperglycemia in the U.S. and found that people with uncontrolled hyperglycemia had a longer length of stay and increased mortality compared with people without diabetes or uncontrolled hyperglycemia. Lim *et al.* (2021) stated that COVID-19 infections have a significant effect on the management of DM because they aggravate inflammation and change the immune system responses, resulting in difficulties with glycaemic control. Patients with DM are more likely to develop cardiorespiratory failure if they have SARS-CoV-2 infection as well as thromboembolism. Patients with DM and COVID-19 are believed to have poorer prognoses as a result of these mechanisms. It is important that patients with DM understand that COVID-19 increases blood sugar levels and that they should strictly follow the clinical guidelines for managing diabetes (Lim *et al.,* 2021).

Recent studies from China and the US, found nearly a third of their patients who died from COVID-19 had DM (Zhou *et al.,* 2020 and Richardson *et al.,* 2020). In particular, DM has a twofold increase in mortality compared to those without DM (Remuzzi and Remuzzi, 2020). People with diabetes are more likely to require invasive mechanical ventilation, be admitted to an ICU, and develop acute kidney injury (Richardson *et al.,* 2020). Longo *et al.* (2020) stated that in a hospital setting, insulin and constant glucose monitoring are the first-choice treatments for hyperglycemia. For non-critically ill hospitalized patients with good nutritional intake, an intensive regimen with basal and prandial insulin analogues is recommended, to achieve the recommended target glucose range of 140–180 mg/dL (Longo *et al.,* 2020). Moreover, the use of intensive insulin therapy was associated with a reduction in inflammatory markers in 451 hospitalized patients with critical illness requiring prolonged intensive care on the ICU in comparison with conventional therapy (Longo *et al.,* 2020). In addition, of the 1200 patients admitted for treatment in the ICU, 203 had diabetes. Intensive insulin therapy was used to reduce the rate of complications, such as newly acquired kidney injury and the need for mechanical ventilation, resulting in a quicker discharge from the ICU and hospital (Longo *et al.,* 2020). Another therapeutic strategy used to treat asymptomatic and non-critically ill COVID-19 patients with T2DM was GLP-1RA, which is a glucose-lowering injective drug used in the treatment of T2DM

and basal insulin (Longo *et al.*, 2020). In comparison with intensive insulin regimens, this combination therapy provides similar glycemic control and lowers the risk of hypoglycemia and weight gain (Longo *et al.,* 2020). An observational, retrospective-case control, multi-center study is currently being carried out, which is aimed to evaluate the effects of Sitagliptin on clinical, laboratory and instrumental parameters during hospitalization for COVID-19 (Fiorina, 2021). However, no data is reported as yet (Fiorina, 2021). Despite the availability of several natural and/ or herbal remedies, little or no scientific evidence is available to show an association between COVID-19 and these remedies (Pinato *et al.,* 2021).

9. Conclusion

Based on the evidence obtained from literature review, DM has a devastating impact on the quality of life and increases the possibility of comorbidities/ complications. Several risk factors, especially the demographic profile of an individual, must be considered when assessing the increased prevalence of T2DM. In addition, due to the limitations in the health care system, DM patients are resorting to various types of TM to control their disease. In order to prevent increasing incidence of DM, further research is needed to improve health information and create tracking capabilities.

CHAPTER THREE

Research methodology

3.1. Study site

This study was conducted at R.K. Khan hospital which is a regional and district hospital located in Chatsworth, a suburb in the eThekwini health district. R.K. Khan has evolved from being a community hospital to one of the four major hospitals in the Durban region. The hospital has a catchment population of over 1500 000 people whom are among the poorest in eThekwini. With only 543 authorized beds, the hospital has approximately 36 000 admissions a year and 600 000 outpatients are treated annually (KZN Department of Health 2019).

3.2. Study design and population

A quantitative cross-sectional study design was used to conduct this study. It was made up of 2 phases.

Phase 1: objective 1

This included a retrospective chart review of all outpatients who were treated for T2DM between the period August 2018- January 2019 at R.K. Khan Hospital. Hospital registers was used to access the data as per the data collection tool.

Phase: objective 2 and 3

This phase was a prospective recruitment of all outpatients who visited R.K. Khan hospital to determine their use of home remedies/ traditional medicine for T2DM. The target population was 45 years and older. Outpatients were selected as the target population because there were no designated department for diabetic patients. All participants had

to be registered on the outpatient register at the hospital and diagnosed with T2DM for 5 years and more.

3.3. Sampling strategy

Permission was sought from DUT ethics committee (IREC), the Department of Health and hospital management (Annexure B, C and D) to conduct the study. Once permission was received, a retrospective review on hospital registers for the period August 2018 to January 2019 was carried out to determine the prevalence of T2DM. Data such as age, gender and ethnicity was collected and electronically captured using a data capturing tool (Annexure E). Purposive sampling technique was used to recruit a total of 350 patients for Phase 2. Phase 2 recruited Indian and African participants in equal numbers.

3.4. Inclusion and Exclusion criteria

Phase 1: Objective 1

Inclusion criteria:

All participants were:

- Treated with T2DM within the 6 months (Aug 2018- Jan 2019) under study
- Reporting to R.K. Khan hospital for chronic treatment

Phase 2: Objective 2 and 3

Inclusion criteria:

All participants were:

- Diagnosed with T2DM for 5 years and more
- 45 years old and above

Exclusion criteria

All participants were:

- Diagnosed with T2DM for less than 5 years
- Below the age of 45 years old

3.5. Data collection

Data was collected in two phases, a retrospective review of the hospital registers which was phase 1 (objective 1) and a structured questionnaire which was phase 2 (objective 2 and 3).

Phase one: objective 1

A retrospective record review of all outpatients who reported to the hospital to be treated for T2DM between the period August 2018- January 2019 was conducted. Patients attended the DM clinic within the district hospital for chronic treatment. Data such as age, sex, ethnicity (race) and any coexisting morbidity was collected from outpatient hospital registers for a period of 6 months and electronically captured using a record review tool. Data was limited by the information available on the hospital register, so clinical data for other related T2DM associated morbidities (e.g. oral, ocular, foot ulcers etc) was not included.

Phase two: objective two and three

A bilingual assistant was employed to translate all relevant documents and trained to assist in administering the questionnaires. The training included all information about the study, communication skills and a confidentially document (Annexure F). Data was collected by means of a structured questionnaire. As the outpatients waited to be assisted, prospective participants were approached and informed of the study (Annexure G), thereafter, participants were given a questionnaire that was administered to them in their preferred language (English or Isizulu) after providing informed consent (Annexure H).

3.6. Measurement instrument

A questionnaire (Annexure I) was used as the measurement instrument in this study and was available in English and IsiZulu. The questionnaire included 3 sections. Section A included a demographic section which collected information such as patients age, level of education and socio-economic status, whilst Section B collected information on the extent and use of home remedies/traditional medicine. Section C provided data on complications and/ or comorbidities related to T2DM.

3.7. Validity and Reliability

Zohrabi (2013: 257) defined validity as an instrument to evaluate what is supposed to or purports to evaluate. It is an essential criterion for assessing the quality and acceptability of research. Reliability, however, is related to the precision and accuracy of the instrument to achieve the aims of the study (Zohrabi 2013: 258). The validity and reliability of the study was maintained by designing questions according to the principles defined by Zohrabi (2013: 258). Each question was accurately phrased to avoid ambiguity and leading respondents to a particular answer. A pilot study was done to confirm the reliability and validity of the study.

3.8. Pilot study

The questionnaire was piloted among 5 patients similar to that of the selected sample population at R.K. Khan hospital following the same procedure of the main study. The pilot study was conducted to determine if any questions were irrelevant or ambiguous and if participants clearly understood the questions. The amended questionnaire was then used for the main study.

3.9. Data analysis

All results obtained from the data collection process was captured on a Microsoft excel spread sheet. STATA version 12 (STATACORP) was used for analysis. This is a statistical software program which includes a broad range of statistical analysis, graphics and data management programs that was used to assist in verifying, categorizing, sorting and summarizing the collected data into logical and appropriate sets of information that is easy to interpret and work with.

Phase 1: objective 1

Descriptive statistics included frequency counts, percentages, mean and standard deviation. T2DM cases from the hospital register was stratified by race, age and gender to determine the demographic profile. There was comparatively fewer Coloureds (mixed ethnicity) and White (Caucasians) patients compared to African and Indian, so they were excluded from further bivariate and multivariate analysis. A test of proportions was used to evaluate differences between demographic variables and sex. Early onset DM is defined as DM diagnosed before 45 years old. The Student's t-Test was used for comparisons for age stratified by sex and pre-existing comorbidities, while the chi-squared test of proportions was used to compare T2DM stratified by sex, race, age and comorbidities. Logistic regression models were run using the comorbidity as the dependent variable and gender and race as the independent variables. Models were adjusted for age. HPT, cardiac problems, epilepsy, asthma, arthritis, anaemia, mental health and TB were designated as dependent variables, while gender and race were dependent variables. Multinomial regression analysis was conducted using the frequency of pre-existing comorbidities as a dependent variable with sex and race (African/Indian) as the independent variables. A p-value ≤ 0.05 was considered statistically significant at a 95% CI.

Phase 2: objective 2 and 3

Responses to the questionnaire was pooled, edited and scored. Nominal values were assigned to the items according to scales. Descriptive statistics included frequency counts, percentage, mean and standard deviation. The Chi-squared and t-test were used to determine the association between socio-demographic variables (age, sex, level of education, income status, etc) and Traditional medicine usage. Multivariate logistic regression was used to determine predictors of Traditional medicine usage as well as the effects of the independent variables (age, sex, lack of exercise, diets, etc.) on the co-existence of complications/ co-morbidities of type 2 diabetes mellitus. Odds ratio and the 95% CI was calculated. A p-value ≤ 0.05 was considered statistically significant.

3.10. Ethical consideration

The following measures was carried out to ensure that the study was conducted in an ethical manner:

- The research proposal was submitted to the DUT's Institutional Research Ethics Committee (IREC) to be reviewed and approved. An ethical clearance number was issued by the DUT IREC (Annexure B)
- All relevant documents and questionnaires were translated in Isizulu for participants who preferred the use of this language.
- Ethical approval was granted by the KZN Department of Health (Annexure C).
- Gatekeepers' permission was sought from the hospital management (Annexure D).
- The research assistant was provided with a document of confidentiality to sign (Annexure F) and the signed copy was issued to them.
- A letter of information that included details of the researcher and the study was provided to prospective participants (Annexure G).
- All respondents were made aware of their rights prior to conducting the study. Participants were informed that participation was strictly voluntary and that they are

allowed to withdraw from the study at any point without consequence. They were also made aware that confidentiality and anonymity would be maintained.

- Informed consent was obtained from all participants involved in the study (Annexure H).

CHAPTER FOUR

Published Manuscript 1

Included as an Appendix

Chetty, L., Govender, N., Govender, G.M. and Reddy, P., 2021. Demographic stratification of Type 2 diabetes and comorbidities in district healthcare in KwaZulu-Natal. *South African Family Practice*, 63(1), a5218.

CHAPTER FIVE

Manuscript 2: Under review

Traditional medicine use among Type 2 Diabetes patients in KZN

Advances in Public Health

Traditional medicine use among Type 2 Diabetes patients in KZN

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Abstract

Background: Traditional medicine (TM) is increasingly used in both developing and developed countries as a result of diabetes mellitus (DM) prevalence. Approximately 53% of South Africans use TM to prevent and treat their diseases, however, there is no conclusive evidence of the safety and effectiveness of TM versus conventional medicine. The most common therapies used by diabetics in Africa include herbal treatments, nutritional products, spiritual healing, and relaxation techniques. Diabetic patients in South Africa appear to use different ways of treating their condition due to varying cultures, environments and ethnicity which is inadequately documented. Evaluating evidence-based practices can help in developing effective treatment plans. Therefore, this study aimed to evaluate the use of TM in patients with T2DM who are on chronic therapy in KwaZulu-Natal.

Method: This cross-sectional study was conducted at a district hospital, in which purposive sampling was used to recruit participants via a structured questionnaire. A total of 340 participants, aged 45 years and older was recruited. Demographic data, information pertaining to the extent and use of home remedies/TM and participants self-care practices whilst using TM was collected.

Results: Of the 340 participants, 72% (n=244) were female. Only 92 (27%) of the 340 participants reported using TM, with Indians being the most frequent users (58.24%). Approximately, 77.69% (n= 101) used TM in conjunction with hospital medication. Most participants (53.79%) received TM knowledge from family. The most frequently used TM were lemon and honey, Aloe veera, bitter gourd, green tea, cinnamon, curry leaves and tulsi leaves. Traditional medicine use among African participants was 0.56 times (OR=0.56, 95% CI=0.34, 0.93) lower than Indian participants. There were no significant predictors for TM usage among the variables tested.

Conclusion: Females were identified as the more frequent users of TM. A significant correlation was noted between ethnicity and TM use. The most widely used type of TM was Ayurveda/herbal remedies. Large scale studies are required to determine the additive and synergistic effects of TM in health care. Consideration should also be given to integrating TM into mainstream healthcare.

Key words: Traditional medicine, home remedies, Traditional complementary and alternative medicine, Type II diabetes mellitus, Prevalence, Ethnicity

Background

Diabetes mellitus (DM) is a chronic disease, caused by insulin deficiency or resistance [1], and describes various distinct metabolic disorders, of which chronic hyperglycemia is the most common [2,3]. Diabetes induced complications, such as heart attack, stroke, kidney disease, amputations, poor vision, and nerve damage, are more likely to occur in hyperglycemic individuals [4]. Global prevalence increased by 130% between 1990 (211.2 million) and 2017 (476 million) [5]. In Africa, the highest estimated prevalence rates are from Nigeria (3.2 million), followed by South Africa (2 million), Kenya (over 0.7 million), and Cameroon (over 0.5 million) respectively [6]. However, in the preceding 8 years since the 2012 report, the prevalence has most likely escalated given the trajectory of DM incidence. Diabetic cases are classified into type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM). T1DM results from the destruction of pancreatic beta cells by

T cells of the immune system [3,7,8], whereas T2DM is characterized by defective insulin secretion by pancreatic β-cells and the inability of insulin-sensitive tissues to react appropriately to insulin [9]. Apart from clinical therapeutics, many DM patients have utilized traditional and complementary alternative medicine (TCAM), strategies to control and manage this disease [10].

Traditional medicine (TM) or alternative/complementary medicine (CAM) refers to practices based on the theories, beliefs, and experiences indigenous to different cultures [11]; and is widely used in the treatment of DM [12,13], in both developed and developing countries. It is important to note that TM is referred to as alternative or complementary medicine in various countries [14]. Almost 40% of those residing in the US use traditional medicine (TM) versus 52.79% living in South Africa [13]. Complementary and alternative medicine (CAM) include a series of health care practices and products [15,16], however, the safety and effectiveness of CAM versus conventional medicine remains inconclusive [17]. Notably, complementary medicine is used in conjunction with conventional therapy [16], whereas alternative medicine replaces conventional medicine [16]. Complementary medicine was perceived to have fewer adverse effects than prescription medication [16]. Recent research shows a 50–80% increase in the use of complementary medicine [18]. Almost 80% of people living in developing countries still depend on CAM [10]. In Sub-Saharan Africa, TCAM is widely used to prevent and treat communicable and non-communicable diseases [19], contributing to almost 2.9 billion to the South African economy alone [20]. In Africa, herbal medicines, nutritional products, spiritual healing and relaxation techniques are frequent CAM therapies used by diabetic patients [21]. A recent systematic review and meta-analysis confirm the use of acupuncture, mind–body therapies, religious and spiritual healing as well as homoeopathic remedies amongst diabetics in various countries such as Saudi Arabia, Nigeria, Turkey, India, Lebanon, US, etc. [22].

A Malaysian study among 240 diabetic patients showed a 62.5% CAM use, with females 1.8 times more likely than males to use CAM [23]. Notably, biological therapy which is a

type of treatment that uses substances made from living organisms to treat a disease and stimulating the body's immune system, was more widely used (50%), followed by manipulative-body based systems (9.2%), energy system (8.8%), alternative medicine systems (4.6%) and mind-body system (1.7%) [23]. Similarly, a Taiwanese cross-sectional survey reported an extensive use of CAM in conjunction with conventional medicines [24]. Before T2DM diagnosis, only 22.7% used CAM, however the prevalence increased to 61% after diagnosis, with nutritional supplements reported as the most commonly used pre and post diagnosis [24]. Post diagnoses, CAM modalities included nutritional supplements, Chinese herbal medicines, diet modifications, manipulative-based therapies, biofield therapy, bioelectromagnetic-based therapies, supernatural healing therapies, and mind-body therapies whereas acupuncture, cupping, and scraping, and aromatherapy remained the same pre and post diagnosis [24].

The wide use of African traditional medicine (ATM) by almost 72% of the Black African population prior to the advent of orthodox medicine has been well established [25]. Several studies confirm cinnamon, ginger, fenugreek, bitter gourd, ivy gourd and crepe ginger as the more frequently used herbal remedies for DM [16,26,27]. In South Africa, the more popular DM herbal remedies include *Vernonia amygdalina* (bitter leaf), *Hypoxis hemerocallidea* (African potatoe), Mimusops zeyheri, *Catharanthus roseus* (Madagascar Periwinkle), and *Sutherlandia frutescens* (cancer bush) [28]. The biological and pharmacological effects of *Aloe Ferox, Artemisia afra and Leonotis leonuris* is extensively reported [29,30,31]. *A. Ferox* improves carbohydrate metabolism and reduces obesity-induced glucose intolerance, whereas *A. afra and L. leonuris* demonstrates hypoglycemic and hypolipidemic effects [28].

Recent data confirm that most of the patient's knowledge regarding TCAM is obtained via family, friends, and social media, suggestive that many fail to consult with medical personnel's regarding their use of TCAM in conjunction with T2DM medication [26,32]. Major medical concern exists regarding the efficacy of prescribed T2DM medication when patients opt to replace prescribed treatment with CAM modalities [33]. However, several

studies support TCAM use in conjunction with clinical treatment, due to its reduced side effects, cost-effectiveness, easier accessibility, and acceptability [23,24], however, many patients opt out of using TCAM because of the lack of scientific data to support its preparation, effectiveness, dosage, and the risk of side effects [34]. Despite the prevailing clinical importance of TCAM usage in the management of DM, further studies investigating the impact of TCAM on DM control and management is warranted [27]. In Africa, it remains unclear how patients manage their diabetes in light of combining TCAM and clinical therapy [35,36]. It was established that there is a lack of information regarding the comparison of treatment approaches and methods used by DM patients due to various cultures and environments in South Africa which has not been well documented [37]. Moreover, there is insufficient studies that have been conducted to make comparisons between the various treatment approaches that are used in KwaZulu-Natal, which is a multi-racial province, where DM is common amongst all race groups with the highest prevalence amongst the Indian population (15.8%), followed by the African (4.8%) and White (3.5%) populations [38]. An evaluation of evidence-based practices may assist in the development of treatment approaches [37]. Therefore, this study aims to evaluate the use of TM in patients with T2DM who are on chronic therapy in KwaZulu-Natal.

Methodology

Study design and site

This cross-sectional study was conducted at a district hospital located in a suburb in the eThekwini health district. The hospital is one of the four major hospitals in the Durban region serving a population of over 1500 000 people, predominately the Indian and African groups from the middle to low socioeconomic strata, who have no access to medical aid. Ethical approval was obtained from the Institutional Research Ethics Committee (REC 112/19) and the KwaZulu-Natal Department of Health. Informed consent was obtained from all participants.

Study population and sample strategy

Purposive sampling was used to recruit a total of 340 patients with equal numbers of Indian and African participants. All outpatients 45 years and older, diagnosed with T2DM for 5 years and more, and who reported to the hospital for treatment were included.

Data collection

Data was collected using a structured questionnaire, inclusive of demographic information including age, sex, level of education and economic status. Information on the extent and use of home remedies/TM as well as participants self-care practices whilst using TM were obtained. This section included questions on participants frequency of visits, the joint use of TM and prescribed medication, the reasons for TM use and the source of information regarding TM. Additionally, the complications and/ or comorbidities related to T2DM was calculated. The validity and reliability of the study was maintained by designing questions according to the principles defined by Zohrabi [29] and piloted before use.

Data analysis

Data was analysed using STATA version 12 (Statacorp). Descriptive statistics including frequency counts and the use of TM was stratified by gender, race, age and relevant comorbidities. The Chi-square and T-test was done to determine the association between socio-demographic variables and TM usage. Multivariate logistic regression was used to determine predictors of TM usage as well as the effects of the independent variables on the co-existence of complications/ co-morbidities of T2DM. Odds ratios and the 95% confidence interval was calculated. A p-value ≤ 0.05 was considered statistically significant.

Results

The socio-demographic and disease-related characteristics of the participants is shown in Table 1. Of the 340 participants, 72% (n=244) were females, with a mean age of 61 years (SD=10.17). Majority of the participants presenting with T2DM were between 45-59 years (47.94%), followed by 60–75-year old's (39.12%). Notably, of the 340 participants, only 92 (27%) participants reported TM usage, with Indians being the more frequent users (58.24%). Traditional medicine usage was more prevalent among those with secondary level of education (58.70%), followed by the unemployed (25%) and retired individuals (21.74%) respectively. Additionally, 91.21% of TM users reside in informal settlements.

Table 1: Demographic profile of Type 2 diabetes mellitus patients stratified by traditional medicine use (N= 340)

		Traditional medicine use	
Characteristics	**Total (n, %)**	**Yes n (%)**	**No n (%)**
Gender			
Male	96 (28.24)	23 (25.00)	73 (29.44)
Female	244 (71.76)	69 (75.00)	175 (70.56)
Race			
Indian	162 (48.36)	53 (58.24)	109 (44.67)
African	173 (51.64)	38 (41.76)	135 (55.33)
Age category (years)			
45 – 59	163 (47.94)	40 (43.48)	123 (49.60)
60 – 75	133 (39.12)	38 (41.30)	95 (38.31)
Above 75	44 (12.94)	14 (15.22)	30 (12.10)
Religion			
Hindu	67 (19.71)	24 (26.09)	43 (17.34)

Muslim	19 (5.59)	6 (6.52)	13 (5.24)
Christian	184 (54.12)	45 (48.91)	139 (56.05)
Other	70 (20.59)	17 (18.48)	53 (21.37)
Educational level			
No education	32 (9.44)	9 (9.78)	23 (9.31)
Primary	117 (34.51)	28 (30.43)	89 (36.03)
Secondary	180 (53.10)	54 (58.70)	126 (51.01)
Undergraduate	7 (2.06)	1 (1.09)	6 (2.43)
Postgraduate	3 (0.88)	0	3 (1.21)
Occupation			
Farmer/labourer	2 (0.59)	0	2 (0.81)
Domestic worker	15 (4.42)	4 (4.35)	11 (4.45)
Housewife	49 (14.45)	19 (20.65)	30 (12.15)
Unemployed	117 (34.51)	23 (25.00)	94 (38.06)
Retail	9 (2.65)	4 (4.35)	5 (2.02))
Retired	76 (22.42)	20 (21.74)	56 (22.67)
Pensioner	38 (11.21)	10 (10.87)	28 (11.34)
Other	33 (9.73)	12 (13.04)	21 (8.50)
Residence			
Informal settlement	309 (91.42)	83 (91.21)	226 (91.50)
Formal housing	29 (8.58)	8 (8.79)	21 (8.50)

*p<0.05 was considered statistically significant

There was missing data in some categories

183

184 The characteristics of the T2DM participants are shown in Table 2. Approximately 40%
185 of all participants (n=135) reported living with T2DM for between 10 to 19 years.
186 Interestingly, 56.21% of all participants reported no family history of DM. High blood sugar
187 levels (HBSL) were most frequently treated by medication only (39.27%), and the

188 interventions used the least for controlling HBSL were diet and exercise. Home monitoring
189 of blood glucose levels was reported by 157 participants (48.61), while 27.06% (n= 92)
190 reported the use of TCAM methods to manage HBGL. The self-care practices of all TM
191 users (n=134) are shown in Table 3. Approximately 35% of participants used TM for more
192 than 5 years. Most respondents (51.91%) indicated that their frequency of TM usage was
193 at least once a day, whereas 15.6% (n=21) reported TM usage twice a day or 3 and 9%
194 (n=13). There was an overwhelming belief among participants that the usage controlled
195 HBSL (91.73%, n=122). However, 33.08% (n=44) felt that TM usage controls the HBSL
196 as well as produces less side effects, whereas 20.30% reported having no other health
197 problems. Moreover, 26.32% (n=35) chose TM usage because of its affordability. Out of
198 123 responses, 88.98% reported the TM use for HBSL. It was disconcerting to note that
199 23 participants reported replacing their hospital prescription with TM usage, whilst 77.69%
200 (n= 101) used TM in conjunction with hospital medication. Most participants (53.79%)
201 received TM knowledge from family, 30.30% reported obtaining knowledge from friends
202 and 28.03% from nurses. Interestingly, 89.31% reported that they would recommend TM
203 to other patients diagnosed with T2DM. In this study the most frequently used TM were
204 *Citrus limonum* and *Apis cerana*, commonly known as lemon and honey, Aloe veera,
205 *Momordica charantia* usually called bitter gourd or karela, *Camellia sinensis* also known
206 as green tea, followed by *Cinnamomum verum*, *Murraya koenigii* or curry leaves and
207 *Ocimum tenuiflorum*, also known as tulsi leaves (Table 4).

208

Table 2: Clinical characterization and self-care activities among Type 2 diabetes mellitus patients (N=340)

	Total n (%)
Period of diagnosis (years) (n=340)	
5 – 9	150 (44.12)
10 -19	135 (39.71)
20 - 29	34 (10.00)

30 - 39	17 (5.00)
40 - 49	4 (1.18)
Family history of high blood glucose levels (HBGL) (n=338)	
No	190 (56.21)
Yes	143 (42.31)
Don't know	5 (1.48)
Treatment of HBGL (n=331)	
Medication only	130 (39.27)
Diet only	6 (1.81)
Diet and medication	21 (6.34)
Diet and exercise	1 (0.30)
Diet, medication and exercise	27 (8.16)
Insulin	16 (4.83)
Medication and insulin	95 (28.70)
Diet, exercise, medication and insulin	32 (9.67)
Diet and insulin	3 (0.91)
Frequency of hospital visits for treatment (n=323)	
Once a week	5 (1.55)
Twice a week	4 (1.24)
Once a month	213 (65.94)
Twice a month	5 (1.55)
Twice a year	67 (20.74)
Four times a year	2 (0.62)
Other	27 (8.36)
BGL checked at home (n=323)	157 (48.61)
Traditional medicine use (n=340)	92 (27.06)

HBGL= High blood glucose level

BGL=Blood glucose level

Table 3: Traditional medicine use among Type 2 diabetes patients (N=340)

TM practices	Total n (%)
Duration of traditional medicine use (n=136)	
< 12 months	8 (5.88)
1 year	31 (22.79)
2-3 yrs	20 (14.71)
3-5 yrs	29 (21.32)
More than 5 yrs	48 (35.29)
Frequency of traditional medicine use (n=131)	
Once a day	68 (51.91)
Twice a day	21 (16.03)
3 or more times a day	13 (9.92)
3 times a week	1 (0.76)
Once a month	3 (2.29)
Less frequent	8 (6.11)
Other	17 (12.98)
Reasons for using traditional medicine (n=133)	
Controls my high blood glucose levels	122 (91.73)
I experience less side effects than my tablets	44 (33.08)
I do not have health problems	27 (20.30)
It's cheap	35 (26.32)
Traditional medicine used when my BGL is high (n=127)	113 (88.98)
Traditional medicine used when my BGL is low (n=123)	69 (56.10)
Satisfied with medication given by hospital (n=116)	96 (82.76)
Hospital medication stopped when taking traditional medicine (n=124)	24 (19.3)
No	100 (80.65)
Yes	23 (18.55)

Sometimes	1 (0.81)
Traditional medicine used in conjunction with hospital medication (n=130)	
No	29 (22.31)
Yes	101 (77.69)
Source of information about traditional medicine (n=132)	
Doctor	8 (6.06)
Pharmacy	4 (3.03)
Magazine	2 (1.52)
Family	71 (53.79)
Friends	40 (30.30)
People waiting in queue	5 (3.79)
Radio	5 (3.79)
Internet	7 (5.30)
Nurses	37(28.03)
Perceived therapeutic effects from the use of traditional medicine (n=133)	
No	3 (2.26)
Yes	114 (85.71)
Not sure	16 (12.03)
Recommend traditional medicine to others (n= 131)	
No	10 (7.63)
Yes	117 (89.31)
Not sure	4 (3.05)

** Out of the 92 participants that use traditional medicine, many of the participants have used more than one traditional medicine, which account for the varying totals.

Table 4: Traditional medicine/ home remedies used (N=92)

Scientific name	Common name	Total n(%)
Ocimum tenuiflorum	Tulsi leave	7 (2.06)
Mangifera Indica	Mango leave	2 (0.59)
Cyrtanthus obliquus and Lippa javanca	Imbiza	6 (1.76)
Momordica charantia	Bitter gourd or karela	12 (3.53)
Cinnamomum verum	Cinnamon	10 (2.94)
Hypoxis hemerocallidea	Zifozonke	2 (0.59)
Murraya Koenigii	Curry leaves	9 (2.65)
Aloe barbadensis miller	Aloe veera	14 (4.12)
Vitis vinifera	Procydin	6 (1.76)
Azadirachta indica	Neem	3 (0.88)
Camellia sinensis	Green tea	11 (3.24)
Moringa oleifera	Drumstick leaves or moringa	7 (2.06)
Zingiber officinale	Ginger	5 (1.47)
Allium sativum	Garlic	5 (1.47)
Citrus limonum and Apis cerana	Lemon and honey	16 (4.71)
Cannabis sativa	Weed or marijuana	4 (1.18)

Traditional medicine usage stratified by co-morbidities before and after diagnosis of T2DM are depicted in Table 5. Of the total 24 comorbidities investigated, a substanstial increase of comorbidities was experienced before diagnosis than after diagnosis. The leading comorbidities before diagnosis were high blood pressure (32.92%), tooth decay and infection (25.39%), vision difficulty (23.43%) and cramps (15.92%). Post diagnosis, the more common comorbidities experienced were dry mouth (82.25%), vision difficulty

(77.02%), dizziness (76.14%), cramps (75%) and high blood pressure (66.45%). A statistically significant increase in participant numbers was noted post diagnosis for numbness of hands (29 to 139), numbness of feet (33 to 149 after diagnosis), arthritis and joint pain (54 to 225); and swelling in feet and legs (25 to 124). These increases were similar regards to adverse changes in sleep cycle (31 to 151) and depression (42 to 119). Of all TM users, 70 reported suffering from dry mouth, 62 reported arthritis and joint pain, 60 experienced cramps, 70 experienced dizziness and 64 reported vision difficulty.

Gender, race, age, educational level, residence, and presence of DM comorbidities were among the factors tested as independent predictors for TM usage. The odds of TM use in female participants were 1.31 times (OR=1.31, 95% CI=0.75, 2.78) higher compared to male participants. Traditional medicine use among African participants were 0.56 times (OR=0.56, 95% CI= 0.34, 0.93) lower compared to Indian participants. The odds of TM use among participants aged between 60 -75 years (OR=1.32, 95% CI=0.78, 2.24) and above 75 years old (OR=1.42, 95% CI=0.67, 3.01) were respectively 1.32 and 1.42 times higher than younger patients. There were no significant predictors for TM usage among the variables tested (Table 6).

Table 5: Comorbidities stratified by T2DM diagnosis and traditional medicine use

Co-morbidities	Before diagnosis n(%)	After diagnosis n (%)	p-value	Frequency of symptoms				No traditional medicine use n(%)	Traditional medicine use n(%)	p-value
				Very often	Often	Seldom	Very seldom			
Tooth decay and infection	81 (25.39)	155 (47.84)	0.000	12 (9.76)	35 (28.46)	47 (38.21)	29 (23.58)	121 (50.84)	34 (39.53)	0.072
losing of teeth	42 (14.74)	170 (58.82)	0.090	9 (9.78)	28 (30.43)	40 (43.48)	15 (16.30)	130 (76.47)	40 (23.53)	0.201
Swollen bleeding gums	27 (10.15)	106 (39.85)	0.000	6 (7.89)	22 (28.95)	29 (38.16)	19 (25.00)	86 (81.13)	20 (18.87)	0.032
Dry mouth	30 (10.27)	241 (82.25)	0.421	13 (9.63)	41 (30.37)	56 (41.48)	25 (18.52)	171 (70.95)	70 (29.05)	0.150
High blood pressure	105 (32.92)	206 (66.45)	0.000	10 (7.75)	35 (27.13)	56 (43.41)	28 (21.71)	156 (75.73)	50 (24.27)	0.115

Chest pain	27 (10.04)	101 (38.40)	0.000	6 (8.45)	16 (22.54)	34 (47.89)	15 (21.13)	77 (76.24)	24 (23.76)	0.472
Heart attack	26 (10.36)	44 (17.81)	0.000	3 (11.11)	4 (14.81)	9 (33.33)	8 (29.63)	34 (77.27)	10 (22.73)	0.595
Athiritis or joint pain	54 (17.65)	225 (72.35)	0.000	46 (32.39)	36 (25.35)	45 (31.69)	15 (10.56)	163 (72.44)	62 (27.56)	0.639
Coldness of feet	35 (12.50)	125 (44.17)	0.000	21 (24.42)	22 (25.58)	33 (38.37)	9 (10.47)	91 (72.80)	34 (27.20))	0.998
Numbness of hands	21 (7.95)	139 (53.46)	0.000	17 (21.25)	24 (30.00)	30 (37.50)	8 (10.00)	102 (73.38)	37 (26.62)	0.678
Numbness of feet	33 (11.83)	149 (52.84)	0.000	24 (22.43)	29 (27.10)	36 (33.64)	18 (16.82)	107 (71.81)	42 (28.19)	0.522
Cramps	50 (15.92)	237 (75.00)	0.142	31 (20.67)	36 (24.00)	54 (36.00)	25 (16.67)	176 (74.58)	60 (25.42)	0.464
Dizziness	32 (10.53)	233 (76.14)	0.589	22 (15.38)	37 (25.87)	55 (38.46)	28 (19.58)	163 (69.96)	70 (30.04)	0.114
Vision difficulty	71 (23.43)	238 (77.02)	0.001	48 (32.21)	56 (37.58)	33 (22.15)	12 (8.05)	174 (73.11)	64 (26.89)	0.499
Problem in sleep cycle	31 (10.54)	151 (51.71)	0.000	27 (24.11)	34 (30.36)	36 (32.14)	14 (12.50)	105 (69.54)	46 (30.46)	0.282
Depression	42 (14.05)	119 (40.20)	0.000	12 (11.65)	15 (14.56)	53 (51.46)	23 (22.33)	85 (71.43)	34 (28.57)	0.624
Weight gain	28 (11.20)	59 (24.08)	0.000	4 (7.41)	14 (25.93)	26 (48.15)	7 (12.96)	48 (81.36)	11 (18.64)	0.115

sweeling in legs and feet	25 (9.03)	124 (43.97)	0.001	17 (20.48)	29 (34.94)	26 (31.33)	11 (13.25)	91 (73.39)	33 (26.61)	0.805
Swelling in abdomen	6 (2.37)	39 (15.85)	0.000	4 (13.79)	11 (37.93)	8 (27.59)	6 (20.69)	30 (76.92)	9 (23.08)	0.739
Hair loss	20 (7.69)	94 (36.72)	0.001	5 (8.93)	19 (33.93)	24 (42.86)	8 (14.29)	67 (71.28)	27 (28.72)	0.706
Slow wound healing	5 (2.07)	59 (24.48)	0.000	3 (16.67)	5 (27.78)	7 (38.89)	3 (16.67)	42 (71.19)	17 (28.81)	0.532
Varicose veins	25 (10.04)	76 (30.65)	0.001	6 (17.65)	14 (41.18)	12 (35.29)	2 (5.88)	49 (64.47)	27 (35.53)	0.035
Anaemia	18 (7.29)	47 (19.50)	0.000	1 (4.76)	5 (23.81)	10 (47.62)	4 (19.05)	33 (70.21)	14 (29.79)	0.478
Ulcers in the foot	8 (3.29)	27 (11.25)	0.000	4 (28.57)	4 (28.57)	3 (21.43)	3 (21.43)	19 (70.37)	8 (29.63)	0.752

#p<0.05

*p<0.005

**A few patients did not know frequency; this was removed from analysis

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Table 6: Predictors of TM use among T2DM patients

Predictors of TM use	OR (95%CI)
Gender	
Male	1.00
Female	1.31 (0.75 - 2.78)
Race	
Indian	1.00
African	0.56 (0.34 - 0.93)
Age category (years)	
45 – 59	1.00
60 – 75	1.32 (0.78 - 2.24)
Above 75	1.42 (0.67 - 3.01)
Religion	
Hindu	1.00
Muslim	0.92 (0.31 - 2.76)
Christian	0.76 (0.38 - 1.50)
Other	0.82 (0.32 - 2.08)
Educational level	
No education	1.00
Primary	0.86 (0.35 - 2.08)
Secondary	1.05 (0.45 - 2.44)
Undergraduate	0.36 (0.04 - 3.47)
Residence	
Informal settlement	1.00
Formal housing	1.09 (0.46 - 2.59)

Family history of HBGL	0.53 (0.33 - 0.86)
Comorbidities	
Tooth decay and infection	0.72 (0.42 - 1.24)
losing of teeth	0.64 (0.37 - 1.12)
Swollen bleeding gums	0.66 (0.35 - 1.24)
Dry mouth	1.61 (0.76 - 3.42)
High blood pressure	0.69 (0.41 - 1.18)
Chest pain	0.92 (0.50 - 1.68)
Heart attack	0.96 (0.44 - 2.14)
Arthritis or joint pain	0.95 (0.54 - 1.67)
Coldness of feet	1.24 (0.71 - 2.18)
Numbness of hands	0.93 (0.53 - 1.62)
Numbness of feet	1.49 (0.84 - 2.64)
Dizziness	1.82 (0.95 - 3.49)
Vision difficulty	0.91 (0.50 - 1.66)
Problem in sleep cycle	1.66 (0.95 - 2.91)
Depression	2.14 (1.04 - 4.39)
Weight gain	0.79 (0.36 - 1.75)
Swelling in legs and feet	1.41 (0.79 - 2.51)
Swelling in abdomen	1.35 (0.56 - 3.25)
Hair loss	1.24 (0.69 - 2.24)
Slow wound healing	1.20 (0.61 - 2.35)
Varicose veins	1.87 (1.02 - 3.45)
Anaemia	1.54 (0.73 - 3.21)
Ulcers in the foot	1.67 (0.65 - 4.29)

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Discussion

Our main findings demonstrate that almost one-third of our diabetic participants reported using home remedies/ TM to manage their condition; whilst females were identified as the more regular users. A significant association was found with ethnicity as Indians used TM more frequently compared to Africans. Although medication was taken as prescribed by most participants, a suitable diet and exercise were not of concern among patients. Majority took their prescribed medication in conjunction with the home remedy/ TM. Common reasons for TM use was that it controls HBSL and 26.32% of participants felt that TM was affordable. Popular TM used included lemon and honey, aloe vera, bitter gourd/ karela, cinnamon, curry leaves and tulsi leaves. Recommendations for TM use emanated mostly from friends and family.

A low prevalence (27.06%) of TM usage among T2DM patients was observed in our study. The CAM usage prevalence rates vary by country and region in patients with T2DM [40,41]. Our findings are comparable with studies from Libiya, Saudi Arabia, US, Lebanon, and India who also yielded low prevalence estimates (29%, 26%, 26%, 38% and 30% respectively) [41,42,43,44,45]. In contrast, the prevalence estimates of CAM use among T2DM patients were higher in Tanzania (78%), Sri Lanka (76%) and Malaysia (63%) [16,23,46]. The varied prevalence rates of CAM usage by region can possibly be explained by the different perceptions of CAM use among various cultures and religions, as well as differences in study design and definition of CAM used per region [47,48]. In the current study, a higher prevalence of TM use was expected especially among the African population. With the rising prevalence of DM amongst the African population, it was assumed that ATM would be frequently used among T2DM patients. The low prevalence observed in our study could possibly be explained by fear for the clinical staff and their reaction towards the use of home remedies/ TM. The hospital setting may have also contributed to the possible lack of disclosure.

Our data also suggests that females are more frequent users of CAM compared males which is consistent with previous reports [24,49,50]. This may be attributed to females being more influenced by cultural beliefs, social beliefs, relatives, etc. A recent Dubai report however highlights males as frequent CAM users, indicating an inconclusive association between sex and CAM use [47]. An earlier study suggested that sex is not a significant factor predicting CAM use in patients with T2DM [51]. Our study found that ethnicity may be a significant factor, since Indians were more likely to use TM compared with the African population. These results were anticipated because DM and CAM use were reported among the Indian population in response to DM in previous reports, however, DM has become a challenge in recent years among the African population. Similar results were obtained from a study conducted in Malaysia [23], where authors reported a deeply rooted multicultural nature and a religious influence in CAM use [23]. According to Raja et al. [32], despite the lack of statistically significant association between ethnicity and TM use, a significant association ($p<0.000$) was noted with female gender, older age, lower education, unemployment, longer duration of diabetes and diabetes-related complication [32].

Several participants in our study treated their HBSL with medication alone (39.27%) followed by medication and insulin (28.70%), while diet and exercise are not prioritized. This data is suggestive of poor diabetes education amongst our participants especially since approximately 40% of our participants had only primary school or no education. Furthermore, following a balanced diet can be expensive and the majority of our TM users (91.21%) lived in informal settlements which may indicate that affordability could be a challenge. Collective DM management should include behavioral modifications as diet plans, avoiding high fat foods, increasing physical activity, glucose monitoring, and foot care [52]. In comparison, a study conducted in the Vellore region of Tamil Nadu, reported a higher adherence to medication (79.80%), as well as good dietary behavior, physical activity, and regular blood sugar monitoring among diabetic patients [53]. Several other studies in Africa indicated an average of approximately 64% of medication adherence

[54,55,56,57], however, moderate compliance to diet plans ranging from 33% to 87% was observed [54,58,59]. Physical activity amongst T2DM patients varied between 29–46 % [54,60,61] and only 15% of patients were able to monitor their blood glucose at home. Similarly, in our study, less than 50% of T2DM patients monitored their blood glucose at home. This may be attributed to the cost of test strips and needles. In addition, many participants were over 60, and may have a negative perception about monitoring their blood glucose levels. In these comparison studies, literacy and easier access to health-related activities may explain the differences in self-care practices. The results of our study suggest that self-management of diabetes is inadequate because even though patients depend greatly on prescription medication they still require a quick healing remedy. Moreover, the self-management inadequacy is particularly due to the lack of physical activity and a healthy diet, both of which pose serious threats to good glycemic control.

Ayurveda was reported as the most common TM modality used by T2DM patients in India [62]. Similar results were obtained from other studies [42,50,63]. For example, bitter gourd (9.09%) and fenugreek seeds (8.18%) were identified as common TM modalities in India since TM alternatives are more widely accepted in rural compared to urban areas [62]. It is possible that similar scenarios apply to our study since the majority of TM users are from informal settlements. The 5 most common TM used in our study were lemon and honey, aloe vera, bitter gourd or karela, green tea, and cinnamon. Bobiş, Dezmirean, and Moise [64] stated that honey has been proven to support hypoglycemia; however, the mechanism of this effect remains unclear. More than 200 substances make up honey, with fructose, glucose, and water being the three main components [64]. In an animal model of diabetes, fructose has been found to reduce blood sugar levels [65]. Additionally, honey might protect the pancreas, which secretes two glucose-regulating hormones known as insulin and glucagon, from oxidative stress [66,67]. There are no hypoglycemic effects of aloe vera, with no conclusive evidence that the supplementation with aloe vera prevents or improves metabolic disorders [68]. Yimam et al. [69] stated that aloe vera

derived extracts can lower cholesterol, prevent insulin resistance, and even prevent diabetes; however, there is still controversy surrounding these findings, making it difficult to draw definitive conclusions. Bitter gourd/ karela's is known for its distinctive taste and nutritional profile and it is eaten as a vegetable throughout the world. It is known to contain vitamin A, C, thiamine, niacin, riboflavin, and minerals [70]. As a result of its of bioactive molecules, bitter gourd exhibits some pharmacological properties, acting as a scavenger of free radicals, a hypoglycemic, and hypolipidemic agent [71]. There is evidence that bitter gourd can be used for diabetes prophylaxis [72,73,74,75]. The presence of alkaloids, flavonoids, saponin, catechins, charantin, vicine, and polypeptide fractions in bitter gourd confirmed its hypoglycemic effect in *in vivo* studies [76]. According to Nei et al. [77], the risk of T2DM is 8% lower in people who drink green tea daily and it reduces mortality risk by 10% among patients with DM, however, the association between green tea consumption and T2DM risk is still inconsistent [77,78]. Furthermore, green tea consumption was associated with a decreased risk of microvascular complications in diabetics such as diabetic nephropathy [77,79]. The bioactive compounds in tea have the ability to influence signal pathways and key molecules involved in the regulation of insulin, blood sugar, and energy metabolism [79]. On the other hand, the biologically active substances in cinnamon, mimic insulin-like properties, including activating insulin kinase, increasing glucose uptake, and auto phosphorylating the insulin receptor [80]. A study conducted by Hong et al. [81] found that the cinnamon peel extract increases insulin sensitivity and raises glucose intake. Bitter apple, cinnamon, and ginger were reported as the more prevalent CAM used in Saudi Arabia [82], in contrast to green tea being used in Jordon [42]; cinnamon in Iran [83], and fenugreek in Sudan [63]. The variations in prevalence rates for the use of different medicinal plants globally may be attributed to the ease of access to medicinal plants and popularity of some medicinal extracts in cooking, for e.g., cinnamon is a common spice sold in most retail stores [50].

The results from this study showed no association between comorbidities and TM use, highlighting a low prevalence of TM use among T2DM patients with comorbidities. Our

findings are corroborated by Vishnu, Mini and Thankappan [45], in which they report that patients without any comorbidity were four times more likely to use CAM compared to patients with comorbidity. A higher prevalence of TM use was predicted in this study, we postulated that the greater the prevalence of comorbidities, the greater the likelihood of TM use, however, contrary results were obtained. This may be attributed to fear of disclosing TM use in a hospital environment or related to the cost of TM. Our findings suggest that most TM users were encouraged by family, followed by friends, and nurses. This is similar to previous reports that relatives and friend are instrumental in shaping an individual's decision regarding the purchase and use of TM [45,84,85,86,87]. It is important that there is involvement of patients' friends and their families during diabetes education counseling regarding the efficacy and potential side effects of CAM use [23]. We also demonstrate that a small number of participants in our cohort use TM as a referral from their health care professionals (6.06%), which corresponds with other reports [47,88]. Radwan et al. [47] reported that only 1 in 4 patients informs their treating physician about the use of CAM, whilst Davis et al. [88] found that there is a lack of communication with health care practitioners. It is possible that sharing their use of CAM is discouraged by fear, i.e. fear of receiving a negative response from the healthcare provider, fear that the practitioner would not continue providing them with healthcare, fear that physicians would discourage CAM use and their perception that the healthcare practitioner does need to know about their use of CAM.

We report the concurrent use of TM with conventional medicines, as previously reported [89,90,91]. In addition to potentially undermining patient safety and health outcomes, the concurrent use of TM and allopathic medicines may result in serious adverse side effects and ineffectiveness of conventional treatments due to drug-herb interactions [19,92]. A study conducted in Pakistan reported that 41% of patients supported the combination of TM and conventional therapy for T2DM and only 3% supported TM use alone [93]. Moreover, our study reports minimal dissatisfaction with conventional medicines (17.24%), which was unexpected, since dissatisfaction with conventional treatments due

to ineffectiveness or extreme side effects were the common reasons for using TM. The main reasons cited in this study for TM use was to control HBGL and fewer side effects, which corresponds to Ching et al. [23] and Chang, Wallis and Tiralongo [24]. Other possible reasons for using TM could be convenience, its organic nature and greater freedom and control in terms of their healthcare choices compared with conventional care.

Study Limitations

While the study was conducted in a regional hospital in KZN, findings cannot be generalized to all areas where DM patients reside, particularly those with access to private health care.

Conclusion

The current study highlighted a low prevalence rate of TM usage (27.06%) in T2DM patients. Traditional medicine was predominately used among females and ethnicity was found to be a significant predictor of TM usage. Ayurveda/ herbal remedies was the most widely used type of TM. Relatives and friends were the main source of TM information. This study warrants the need for health education programs regarding the use of TM, emphasizing proper use, with regard to additive and synergistic effects. It is imperative for health authorities across Africa to evaluate and create a therapeutic space for TCAM, with regard to its role and potential use in healthcare. Consideration should be given to integrating TCAM into mainstream health care in a controlled manner.

Data availability:

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declares that there is no conflict of interest regarding the publication of this article.

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CHAPTER SIX

Summary, conclusion, and recommendations

6.1. Summary

The global increase in DM prevalence, especially in developing countries remains a major public health challenge in Sub-Saharan Africa; and may be attributed to inadequate funding, limited therapeutic access and a disparity in resource distribution between the public and private sectors. Limited access to health care resources restricts the healthcare system in dealing with the rising prevalence, incidence, and complications of DM. It is well established that DM is a chronic NCD that affects approximately 4.5 million people in South Africa (SA) (IDF, 2019), and is estimated to reach pandemic levels by 2030 (Shaw et al., 2010). In SA, the incidence of T2DM is greater in KZN than the other provinces which has previously been attributed to the large Indian population residing in this region. Moreover, the increases in TM use and its complications associated with T2DM is a major concern in DM management. Therefore, this study aimed to determine the demographic profile of T2DM patients in a regional hospital in KZN stratified by age, gender, and race. The use of TM among T2DM patients and the extent of DM related complications and/or co-morbidities among patients with pre-existing T2DM was also assessed. Population-level interventions, particularly those aimed at prevention, may be an avenue to curtail South Africa's burgeoning DM epidemic. However, this type of initiative, may be hindered by the lack of epidemiological data, which is a common issue in most African countries (Atun *et al.,* 2017). The summary data obtained from the regional hospital under study was not previously analysed in terms of stratifying cases by demographics and evaluating co-morbidity risks. Thus, the rationale for this study was to contribute to the current knowledge regarding the DM burden amongst these vulnerable populations, especially since the profile of risk is considered to have shifted over the last decade.

Our findings demonstrate a significantly higher number of female patients (3072) with T2DM, who access hospital treatment compared to males (1050) ($p<0.001$), irrespective of age and sex. The higher T2DM prevalence amongst females may be attributed to sociocultural factors including gender differences in behavioral patterns, which affect nutrition, daily lifestyles and attitudes toward treatment and prevention. Our findings suggest that women seek health care more frequently than men, particularly for chronic diseases. This increase in health-seeking behavior amongst females may be linked to sociocultural and socioeconomic factors. Bivariate and multivariate analysis highlights significantly more Indian female patients presenting with T2DM compared with African females ($p<0.05$).

The most frequent comorbidities experienced in this cohort included hypertension (n=3212) and cardiovascular morbidities (n=460), with a prevalence of 77.9% and 11.16%, respectively. There was a significant increase in the prevalence of comorbid conditions with increasing age; most patients aged 55 to 74 years presented with hypertension, cardiovascular issues, and arthritis ($p<0.05$). Female patients with T2DM were at significantly higher risk of presenting with hypertension (odds ratio [OR] =1.44, 95% CI:1.20;1.71), arthritis (OR = 2.20, 95% CI:1.51;3.20) and anaemia (OR =2.42, 95% CI:1.40;4.19), whilst their risk for cardiovascular problems was significantly lower compared to male patients (OR = 0.67, 95% CI: 0.54;0.83). Notably, women experienced more comorbidities than men, with 84% of them (2574/3072) suffering from both DM and at least 1 or 2 comorbid conditions. Comorbidities presented by Indians were significantly higher than those of Africans, however, Indians were overrepresented in the population under study. Thus, logistic regression showed a greater risk of disease burden amongst Indians compared to Africans, particularly with respect to hypertension. When the presence of multiple morbidities was further stratified by sex, significantly more Indian male patients presented with DM+1 morbidity compared to African male patients. Overall, the 12.5% crude prevalence of T2DM in KZN was higher than the 9.2% national prevalence. This may be attributed to the large Indian population (South Asian) residing in KZN in contrast to other SA cities and is suggestive of a possible genetic predisposition to T2DM.

In phase 2 of our study, only 92 (27%) out of 340 participants reported TM usage, with Indians being the more frequent users (58.24%). This variation may be due to cultural and religious beliefs. Ethnicity was a significant risk factor, since Indians were more likely to use TM compared with the African population. Also, participants with a lower educational level were more likely to use TM. Our findings also revealed diet and exercise as the least used interventions for T2DM which was concerning and warrants further investigation for health education intervention. Approximately, 89% of participants reported TM use for high blood sugar levels, however, it was disconcerting that 23 participants reported replacing hospital prescriptions with TM usage, whilst 77.69% (n=101) used TM in conjunction with hospital medication. This suggests that poor DM education exists amongst our cohort and self-management of T2DM is inadequate. The most frequently used TM included lemon and honey, Aloe vera, bitter gourd or karela, green tea, followed by cinnamon, curry leaves and tulsi leaves. Ayurvedic use is more convenient since it provides the patient with freedom and control over healthcare decisions, and it is organic in nature. Several factors including gender, race, age, educational level, residence, and presence of DM comorbidities were evaluated as independent predictors for TM usage, but none were confirmed as significant predictors.

Sex, ethnicity, and age were identified as critical determinants associated with the prevalence of T2DM and comorbidities. In order to improve accuracy in the prediction of T2DM prevalence, complications, morbidity and mortality, demographic data is essential. Our data highlights the need for the development of health education programs that incorporates potential advantages and disadvantages of TM use. The development of TCAM policies, promoting TCAM research and training, and considering integrating TCAM into mainstream health care is essential.

6.2. Conclusion

T2DM has reached epidemic proportions and is one of the major causes of morbidity and mortality worldwide. The burden of T2DM can be lowered substantially with intensive, multifactorial intervention to target hyperglycemia, the hallmark of the

disease, as well as hypertension and hyperlipidemia, which often coexist with T2DM. The diagnosis and management of T2DM is challenging, hence it is important to consider factors such as age, sex and ethnicity when using HbA1c for diagnosing diabetes. Once T2DM is diagnosed, optimal patient care is essential to avoid complications. Clinical care may be fortified by alternative strategies such as TM based on it popularity in KZN. Medicinal herbs which are extensively used in alternative and complementary medicine systems, forms part of the rich source of traditional medicine DM remedies. Moreover, the findings of this study confirm that T2DM patients use TM to control their high blood sugar levels and because of the fewer side effects experienced. Off note, most of these patients were informed of the benefits of home remedies/TM use from their friends and family rather than their doctors. Hence, many patients are using home remedies/ TM in conjunction to their prescribed medication.

The biological mechanisms through which herbal therapies resolve T2DM is evolving and may be related with modulation of multiple metabolic pathways. Based on safety and their multiple targeting actions, herbal therapies may be considered as potent therapeutic options in managing T2DM. The availability of systematic data regarding the structure, activity, and mode of action of the TM plants and compounds will improve their potential in the development of antidiabetic drugs. Additionally, improving DM data collection by health care systems will advance the precision in prediction of incidence, complications and mortality associated with the disease. This will provide health care systems with the relevant health information and develop tracking proficiencies necessary to prevent the exponential growth of patients afflicted by diabetes.

6.3. Recommendation

Based on the study findings, the following suggestions are made to improve the current health care system:

- Develop diabetes management training programs that include prevention, evaluation, and treatment of complications instead of relying only on glycemic control and symptomatic treatment.

- Early diagnosis and control of hyperglycemia are essential, in preventing long-term complications from T2DM, which can be achieved by using national guidelines and screening tools.

- Introduction of new models of care, such as mobile health programs, to offer specialized screenings for chronic conditions, such as diabetes, which require more than a routine prescription or visit to the hospital.

- Increase the availability and access to culturally appropriate T2DM services, since cultural beliefs and values contribute to knowledge, attitudes, and practices regarding health improvement and management of T2DM.

- In vitro and in vivo studies should be conducted to identify bioactive compounds of traditional medicines, in order to determine their effectiveness at a physiological level. Active ingredients and their molecular interactions are critical to understanding the therapeutic efficacy of the product, as well as standardizing the product.

- The use of TM among T2DM patients must be acknowledged by the patients' health care system, to ensure monitoring of treatment methods, and prevention of defaulting on their treatment plans.

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Annexure A: Proof of submission to Advances in Public Health journal

Dear Dr. Chetty,

Congratulations, the manuscript titled "Traditional medicine use among Type 2 Diabetes patients in KZN" has been successfully submitted to Advances in Public Health.

We will confirm this submission with all authors of the manuscript, but you will be the primary recipient of communications from the journal. As submitting author, you will be responsible for responding to editorial queries and making updates to the manuscript.

In order to view the status of the manuscript, please visit the manuscript details page.

Thank you for submitting your work to Advances in Public Health.

MANUSCRIPT DETAILS

Kind regards,
Jomil Percil
Advances in Public Health

Annexure B: Ethical clearance from IREC

DUT
DURBAN
UNIVERSITY OF
TECHNOLOGY

Institutional Research Ethics Committee
Research and Postgraduate Support Directorate
2nd Floor, Berwyn Court
Gate 1, Steve Biko Campus
Durban University of Technology

P O Box 1334, Durban, South Africa, 4001

Tel: 031 373 2375
Email: lavishad@dut.ac.za
http://www.dut.ac.za/research/institutional_research_ethics

www.dut.ac.za

5 November 2019

Ms L Chetty
64 Road 716
Montford
Chatsworth
4092

Dear Ms Chetty

Prevalence, Traditional medicine use and Co-morbidities among type 2 diabetes mellitus in outpatients- a cross sectional hospital-based survey in KwaZulu-Natal.
Ethical Clearance number IREC 112/19

The Institutional Research Ethics Committee acknowledges receipt of your final data collection tools for review.

We are pleased to inform you that the data collection tools have been approved. Kindly ensure that participants used for the pilot study are not part of the main study.

In addition, the IREC acknowledges receipt of your gatekeeper permission letters.

Please note that FULL APPROVAL is granted to your research proposal. You may proceed with data collection.

Any adverse events [serious or minor] which occur in connection with this study and/or which may alter its ethical consideration must be reported to the IREC according to the IREC Standard Operating Procedures (SOP's).

Please note that any deviations from the approved proposal require the approval of the IREC as outlined in the IREC SOP's.

Yours Sincerely,

Professor J K Adam
Chairperson: IREC

Annexure C: letter of permission to KZN Department of Health research office

Ms. Lauren Chetty

Durban University of Technology

Department of Community Health Studies

Durban

4000

13 May 2019

To: The KZN Department of Health research office

RE: REQUEST FOR PERMISSION TO CONDUCT A RESEARCH STUDY

Dear Sir/Madam

I am a registered master's student of Health Science from the Department of Community Health Studies at the Durban University of Technology. I would like to request permission to conduct a retrospective, cross sectional research study at the Outpatient clinics, RK Khans Hospital. The study is entitled *"Prevalence, traditional medicine use and co-morbidities among type 2 diabetes mellitus in outpatients- a cross sectional hospital-based survey in KwaZulu-Natal".* Diabetes is one of the major non communicable diseases (NCDs) associated with disease burden worldwide, with almost 80% of the mortality occurring in low- and middle-income countries. Based on this premise, it is possible that the prevalence of multimorbidity associated with NCDS is likely to increase as the populations age.

The main aim of the study is to determine the prevalence, extent of traditional medicine use and co-morbidities among type 2 diabetes mellitus in a regional hospital in KwaZulu-Natal.

The objectives of this study are to:

1. To determine the prevalence of type II diabetes mellitus between August 2018 – February 2019 in a regional hospital in KZN

2. To assess the use of traditional medicine among diagnosed type II diabetic patients in a regional hospital.

3. To determine the extent of diabetes related complications and/or co-morbidities among patients with pre-existing type II diabetes mellitus in a regional hospital.

Ethical clearance for the study is currently being sought from the institutional ethics committee (DUT IREC). I humbly request your permission to access the hospital registers at the Outpatient clinics at RK Khans hospital as well as administer an epidemiological questionnaire to the outpatients who wish to voluntarily participate. We will ensure that ethical approval is granted by IREC before commencement of the project. The full proposal together with all questionnaires are available upon request for your perusal.

Your support and permission to conduct the study at RK Khans hospital will be appreciated.

Yours sincerely

Ms. Lauren Chetty

Ms L Chetty	Prof P Reddy	Dr N Govender
MHSc student	Supervisor	Co-supervisor
Tel: 071 643 9096	Tel: 031 373 2808	Tel: 031 373 2796
Email:laurenchetty04@gmail.com Email:nalinip@dut.ac.za		Email:PoovieR@dut.ac.za

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

Physical Address: 330 Langalibalele Street, Pietermaritburg
Postal Address: Private Bag X9051
Tel: 033 395 2805/ 3189/ 3123 Fax: 033 394 3782
Email:
www.kznhealth.gov.za

DIRECTORATE:
Health Research & Knowledge Management

NHRD Ref: KZ_201909_024

Dear Ms L. Chetty
DUT

Approval of research

1. The research proposal titled **'Prevalence, traditional medicine use and co-morbidities among type 2 diabetes mellitus in outpatients - a cross sectional hospital based survey in KZN'** was reviewed by the KwaZulu-Natal Department of Health.

   The proposal is hereby **approved** for research to be undertaken at RK Khan Hospital.

2. You are requested to take note of the following:
   a. Kindly liaise with the facility manager BEFORE your research begins in order to ensure that conditions in the facility are conducive to the conduct of your research. These include, but are not limited to, an assurance that the numbers of patients attending the facility are sufficient to support your sample size requirements, and that the space and physical infrastructure of the facility can accommodate the research team and any additional equipment required for the research.
   b. Please ensure that you provide your letter of ethics re-certification to this unit, when the current approval expires.
   c. Provide an interim progress report and final report (electronic and hard copies) when your research is complete to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za

For any additional information please contact Mr X. Xaba on 033-395 2805.

Yours Sincerely

Dr E Lutge
Chairperson, Health Research Committee
Date: 09/10/19

Fighting Disease, Fighting Poverty, Giving Hope

Annexure D: letter of permission to hospital management

Ms. Lauren Chetty

Durban University of Technology

Department of Community Health Studies

Durban

4000

13 May 2019

To: RK Khan Hospital management

RE: REQUEST FOR PERMISSION TO CONDUCT A RESEARCH STUDY

Dear Sir/Madam

I am a registered master's student of Health Science from the Department of Community Health Studies at the Durban University of Technology. I would like to request permission to conduct a retrospective, cross sectional research study at the Outpatient clinics, RK Khans Hospital. The study is entitled *"Prevalence, traditional medicine use and co-morbidities among type 2 diabetes mellitus in outpatients- a cross sectional hospital-based survey in KwaZulu-Natal".* Diabetes is one of the major non communicable diseases (NCDs) associated with disease burden worldwide, with almost 80% of the mortality occurring in low- and middle-income countries. Based on this premise, it is possible that the prevalence of multimorbidity associated with NCDS is likely to increase as the populations age.

The main aim of the study is to determine the prevalence, extent of traditional medicine use and co-morbidities among type 2 diabetes mellitus in a regional hospital in KwaZulu-Natal.

The objectives of this study are to:

1. To determine the prevalence of type II diabetes mellitus between August 2018 – February 2019 in a regional hospital in KZN

2. To assess the use of traditional medicine among diagnosed type II diabetic patients in a regional hospital.

3. To determine the extent of diabetes related complications and/or co-morbidities among patients with pre-existing type II diabetes mellitus in a regional hospital.

Ethical clearance for the study is currently being sought from the institutional ethics committee (DUT IREC 112/19). I humbly request your permission to access the hospital registers at the Outpatient clinics at RK Khans hospital as well as administer an epidemiological questionnaire to the outpatients who wish to voluntarily participate. We will ensure that ethical approval is granted by IREC before commencement of the project. The full proposal together with all questionnaires are available upon request for your perusal.

Your support and permission to conduct the study at RK Khans hospital will be appreciated.

Yours sincerely

Ms. Lauren Chetty

Ms L Chetty	Prof P Reddy	Dr N Govender
MHSc student	Supervisor	Co-supervisor
Tel: 071 643 9096	Tel: 031 373 2808	Tel: 031 373 2796
Email:laurenchetty04@gmail.com Email:nalinip@dut.ac.za		Email:PoovieR@dut.ac.za

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

DIRECTORATE:
R.K. KHAN HOSPITAL
OFFICE OF THE CEO

Physical Address : R.K. Khan Circle
Physical Address : CHATSWORTH
Tel: [031] 4596001 Fax:[031] 4011247 Email:Dianne.naicker@kznhealth.gov.za
www.kznhealth.gov.za

ENQUIRIES: DR D. BEHADAR

19 SEPTEMBER 2019

MS L. CHETTY
64 ROAD 716
MONTFORD
CHATSWORTH
4092

Dear Ms Chetty

RE: PERMISSION TO CONDUCT RESEARCH: PREVALENCE, TRADITIONAL MEDICINE USE AND CO-MORBIDITIES AMONG TYPE 2 DIABETES MELLITUS IN OUTPATIENTS – A CROSS SECTIONAL HOSPITAL BASED SURVEY IN KWAZULU-NATAL

Permission is granted to conduct the study at this institution.

Please note the following:

1. Please ensure that you adhere to all the policies, procedures protocols and guidelines of the Institution with regards to this research.
2. Please ensure this office is informed before you commence your research and your University's Ethics approval must be attached.
3. **You will be expected to provide feedback on your findings to this institution.**
4. You will be liaising with: Dr M.N. Govender
   Clinical Manager - OPD
   Tel: [031-4596416]

Yours faithfully

DR G.M. GOVENDER
ACTING CHIEF EXECUTIVE OFFICER
/SN

Annexure E: Data collection tool for objective 1

STUDY ID	DATE	AGE	SEX	RACE

Annexure F: Research assistant confidentiality agreement

Study Topic: Traditional medicine use and co-morbidities among type 2 diabetes mellitus in outpatients - a cross sectional hospital-based survey in KwaZulu-Natal.

I, _____ **[name of research assistant]**, agree to assist _____ **[name of principal investigator]**, with this study by handing out questionnaires to participants and providing them with relevant information of the study. I agree that I will:

- keep all research information shared with me confidential by not discussing or sharing the information in any form or format with anyone other than the principle investigator of this study.
- keep all research information in any form or format secure while it is in my possession. This will include the safe keeping of all completed questionnaires in a locked cupboard at DUT
- provide all research information obtained during the research, in any form or format to the principal investigator when I have completed the research tasks.
- not divulge any information obtained from the participant such as name, age, or responses after the completion of the research task.

_____ _____

Signature of the research assistant **Date**

Email:

Phone Number:

_____ _____

Signature of the principal investigator **Date**

Annexure G: letter of information: participants

Warm greetings!

My name is Lauren Chetty. I am a registered Master's student in the faculty of Health Sciences, Durban University of Technology. I would like to invite you to participate in a study that I am conducting regarding high blood sugar levels.

Title of the Research Study: Traditional medicine use and co-morbidities among type 2 diabetes mellitus in outpatients- a cross sectional hospital-based survey in KwaZulu-Natal.

Principal Investigator/researcher: Lauren Chetty

Co-Investigator/s/supervisor/s: Professor P Reddy and Dr N Govender

Brief Introduction and Purpose of the Study: High sugar levels is a problem that is affecting our health care system. Many people in KwaZulu- Natal are suffering with high sugar levels. People who have high sugar levels use lots of home remedies to control their sugar levels. However, they also experience many other health problems. The aim of this study is to therefore find out what home or traditional remedies you use in addition to the medication that you get from the hospital. We also want to find out what other health problems you have besides high sugar levels.

Outline of the Procedures: If you agree to participate in this study, you will have to complete a consent form and thereafter answer some questions that I will ask you while you wait to be attended to in the hospital. The approximate time taken to answer the questions that I ask you is 15 minutes. You are welcome to stop me at any time to ask questions or withdraw if you are uncomfortable being asked any questions.

Risks or Discomforts to the Participant: There is no discomfort or risks that will be experienced during this study.

Benefits: This study will help us to find out what are the different home remedies that people use to control high sugar levels and determine if these remedies are beneficial or not. The study will also determine the various other health problems that may be related to high sugar levels. The results of the study will be used to create awareness among patients with high sugar levels.

Reason/s why the Participant May Be Withdrawn from the Study: Participation in this study is completely voluntary. You are free to withdraw from this study for any reason, and there will be no consequences.

Remuneration: You will not receive any money or reward at the end of the process.

Costs of the Study: You will not be expected to pay any costs relating to this study.

Confidentiality: Your name will not be used in the study.

Research-related Injury: There will be no injury or harm caused by the study, as you are only required to answer the questionnaire.

Persons to Contact in the Event of Any Problems or Queries: You can contact Lauren Chetty (the researcher) on 071 643 9096, Prof P Reddy (supervisor) on 031 373 2808 at the Durban University of Technology, Dr N Govender (co-supervisor) on 031 373 2796 or the Institutional Research Ethics Administrator on 031 373 2375. Complaints can be reported to the DVC: Research, Innovation and Engagement Prof S Moyo on 031 373 2577 or moyos@dut.ac.za.

General: The identities of all participants will be protected throughout the study and even after the study.

Annexure G: Incwadi yolwazi

Sanibonani!

Igama lami nguLauren Chetty. Ngiwumfundi weMasters kumnyango wezempilo, eDurban University of Technology. Ngithanda ukunimema ukuthi ubambe iqhaza kucwaningo engilwenzayo mayelana namazinga aphezulu kashukela kubantu abanesifo sika shukela.

Isihloko socwaningo: Ukusetshenziswa kwamakhambi esinto nawase khaya kubantu abanesifo sikashukela (type 2 diabetes mellitus) imibuzo igxile ezibhedlela eziKwaZulu-Natal.

Umhloli omkhulu/umcwaningi: Lauren Chetty

Abahloli/ababhekelele: Professor P Reddy and Dr N Govender

Isingeniso nenhloso yocwaningo: Izinkinga zashukela onyukile zibonakala ezigamekweni eziningi ezindaweni zempilo. Abantu abaningi KwaZulu- Natal banenkinga yamazinga aphezulu oshukela. Abantu abanenkinga yokukhushukelwa ushukela basebenzisa amakhambi abo ukugcina amazinga kashukela esesimeni. Kodwake, bazithola sekuvumbuka nezinye izinkinga zempilo. Inhloso yalolucwaningo ukuthola ukuthi yimaphi amakhambi abantu abawasebenzisayo ngaphezulu kwalawo asuke bewanikwe esibhedlela. Sihlose ukuthola futhi ukuthi iziphi ezinye izinkinga ezivelayo uma besebenzisa lamakhambi.

Inqubo yohlelo: Uma uvuma ukuba yingxenye yalolucwaningo, kuzomele ugcwalise ifomu eshoyo ukuthi uyavolontiya futhi awuphoqelwekile bese emva kwayo uphendula imibuzo elandelayo, ozobuzwa yona uma usalindile kulayini wokobona udokotela esibhedlela, ukhona ozokubuza. Ngeke kweqe emezuzwini ewu 15 uma ubuzwa. Uvumelekile ukumisa noma ngabe inini ungabe usaqhubeka nokubuzwa uma uzwa ngathi awusathandi noma uhlobo lwemibuzo ebuzwayo ayihambisani nawe.

Ukungaphatheki kahle kwabangenele ucwaningo: Abukho ubungozi nokungaphatheki kahle kwabangenele lolucwaningo.

Inzuzo: Lolu cwaningo luzosiza ekutheni kwaziwe amakhambi abantu abawasebenzisayo ukulawula amazinga kashukela emzimbeni yabo, bese ibheka ukuthi ngabe lamakhambi akulungele yini ukusetshenziswa futhi awadali yini izinkinga ngokuhamba kwesikhathi. Imiphumela izosetshenziswa ukwenza isixwayiso kubantu abanenkinga yamazinga aphezulu kashukela.

Izizathu ezingenza ababambe, iqhaza kulolucwaningo bangaqedi: Akuphoqelekile ukuba yingxenye yalolucwaningo, umuntu uvumelekile ukuyeka noma yinini ukuba yingxenye akunamigomo namibandela.

Inkokhelo: Ayikho inkokhelo etholakalayo ngokuba yingxenye yocwaningo.

Izindleko: Akukho mali ezocelwa kuwe noma okumele uyikhokhe.

Ukugcinwa kwemfihlo: Yonke imininingwane iyogcinwa iyifihlo, igama lakho angeke libhalwe ezimpendulweni ozinikile, lezimpendulo ziyosetshenziselwa lolucwaningo kuphela.

Ukulimala okungenzeka ngenxa yogcinongo: Akukho ukulimala okungenzeka kuloluhlobo locwaningo.

Ongabathinta uma kunezikhalazo noma imibuzo: Naba ongabathinta

Thinta umcwaningi uLauren Chetty (ucingo 071 643 9096), induna yomcwaningi uProf P Reddy (ucingo 031 373 2808) eDurban University of Technology, obambisene nenduna yocwaningo Dr N Govender (ucingo 031 373 2796) noma uthinte i-Institutional research ethics administrator ku-031 373 2375. Izikhalazo zingabikwa kuDirector: Research and Postgraduate support, Prof S Moyo on 031 373 2577 or moyos@dut.ac.za.

Okujwayilekile: Imininingwane yalabo ababeyingxenye yalolucwaningo izovikelwa

Annexure H: INFORMED CONSENT

Statement of Agreement to Participate in the Research Study:

- I confirm that I have been informed by the researcher, Ms Lauren Chetty, about the nature, conduct, benefits and risks of this study - Research Ethics Clearance Number _____.
- I have also received, read and understood the Participant Letter of Information regarding the study.
- I am aware that the results of the study, including personal details regarding my sex, age, date of birth, physical address and my name will be anonymously processed into a study report.
- In view of the requirements of research, I agree that the data collected during this study can be processed in a computerised system by the researcher.
- I may, at any stage, without prejudice, withdraw my consent and participation in the study.
- I have had sufficient opportunity to ask questions and (of my own free will) declare myself prepared to participate in the study.
- I understand that significant new findings developed during the course of this research which may relate to my participation will be made available to me.

_____ _____ _____ _____

Full Name of Participant Date Time Signature / Right Thumbprint

I, Lauren Chetty, herewith confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

_____ _____ _____

Full Name of Researcher Date Signature

_____ _____ _____

Full Name of Witness (If applicable)	Date	Signature
_____	_____	_____
Full Name of Legal Guardian (If applicable)	Date	Signature

Annexure H: IFOMU LEMVUME

Isitatimende Sesivumelwane Sokubamba iqhaza Ocwaningweni:

- Ngiyaqinisekisa ukuthi ngitshelwe umcwaningi, uSolwazi P Reddy mayelana nohlobo, ukuziphatha, izinzuzo kanye nezincuphe zalolu cwaningo – Inombolo Yokususwa Kwezimiso Zokucwaninga: _____,
- Ngilutholile, ngafunda futhi ngaqonda ulwazi olubhalwe ngenhla (Incwadi yombambiqhaza yolwazi) olumayelana nocwaningo.
- Ngiyazi ukuthi imiphumela yocwaningo, kuhlanganise nemininingwane yami mayelana nobulili bami, ubudala, usuku lokuzalwa, izinhlamvu zokuqala zamagama kanye nokutholakala kwesifo kkuyocutshungulwa ngokungalivezi igama lami embikweni wocwaningo.
- Ngokubheka izimfanelo zocwaningo, ngiyavuma ukuthi imininingwane eqoqwe ngesikhathi salolu cwaningo ingacutshungulwa ngohlelo lwekhompyutha ngumcwaningi.
- Ngingakwazi, nganoma yisiphi isigaba, ngaphandle kokubandlulula, ngihoxise imvume yami nokuhlanganyela kulolu cwaningo.
- Ngike ngaba nethuba elanele lokubuza imibuzo futhi (ngokuzithandela kwami) ngingasho ukuthi ngikulungele ukubamba iqhaza kulolu ucwaningo.
- Ngiyaqonda ukuthi lokho okubalulekile okusha okutholakele kwathuthukiswa ngesikhathi salolu cwaningo olungase luhambisane nokubamba kwami iqhaza ngiyokwaziswa khona.

Mina, _____, ngalokhu ngiyaqinisekisa ukuthi umbambiqhaza ongenhla uye waziswa ngokugcwele ngohlelo, ukuziphatha kanye nezincuphe zocwaningo olungenhla.

_____	_____	_____	_____
Igama eliphelele lombambiqhaza	Usuku	Isikhathi	Isignesha/Ukuginqa Isithupha sesokudla

_____	_____	_____

Igama eliphelele lomcaningi Usuku Isignesha

_____ _____ _____

Igama eliphelele lofakazi Usuku Isignesha
(uma ekhona)

_____ _____ _____

Igama eliphelele lombheki Usuku Isignesha
Osemthethweni (uma ekhonma)

Annexure I: Questionnaire for objective 2 and 3

TRADITIONAL MEDICINE USE AND CO-MORBIDITIES AMONG TYPE 2 DIABETES MELLITUS OUTPATIENTS - A CROSS SECTIONAL HOSPITAL BASED SURVEY IN KWAZULU-NATAL

Instructions to the participant:

- Please complete the questionnaire with the black or blue pen provided.
- Questions should be answered by ticking the appropriate block.
- If you make a mistake when answering a question, neatly cross out the incorrect answer and then re-tick the correct answer for that question.
- If a reason is required for your answer, please write it in the space provided
- Please answer all questions as honestly as possible and to the best of your ability. All information provided will be used to create diabetes awareness in the hospital.

Completing this questionnaire is voluntary and all your responses will be strictly confidential.

SECTION A: DEMOGRAPHICS

1. Gender:

Male ☐ Female ☐ Other ☐

2. What is your age? _____ years

3. Race: _____

4. Religion:

Hindu ☐ Muslim ☐ Christian ☐ Other ☐

If other, please specify: _____

5. Level of education:

No education ☐ Primary ☐ Secondary ☐

Undergraduate ☐ Postgraduate ☐

6. What is your occupation?

Farmer/ Labourer ☐ Domestic worker ☐ Housewife ☐

Unemployed ☐ Retail ☐ Retired ☐ Other ☐

If other, please specify: _____

7. Do you live in an:

Informal settlement ☐ or Formal housing ☐

8. Do you have water in your home?

Yes ☐ or No ☐

9. Do you have electricity in your home?

Yes ☐ or No ☐

10. How many years ago were you diagnosed with high blood sugar levels? _____

11. Does anyone in your family have high blood sugar levels?

Yes ☐ No ☐ I don't know ☐

12. Tell me whom? _____

13. Treatment of high blood sugar levels:

Medication only ☐ Diet only ☐ Diet and medication ☐

Diet and exercise ☐ Diet, medication and exercise ☐ Insulin ☐

Medication and insulin ☐

14. How often do you come to the hospital for your treatment?

Once a week ☐ Twice a week ☐ Once a month ☐

Twice a month ☐ Other ☐

If other, please specify: _____

15. Do you check your blood sugar levels at home?

Yes ☐ or No ☐

16. If yes, how do you check it? _____

17. What do you do when your blood sugar levels are high?

_____

_____

18. How do you know when your blood sugar levels are high?

_____

_____

19. What do you do when your blood sugar levels are low?

_____

_____

20. How do you know when your blood sugar levels are low?

_____

_____

SECTION B: USE OF HOME REMEDIES/ TRADITIONAL MEDICINE

1. Do you use other ways to control your high blood sugar levels, other than the medication you get from the hospital?

   Yes ☐ or No ☐

If YES, please answer Question 2, and thereafter proceed to section C.

If NO, proceed to Question 3, and thereafter proceed to section C.

2. What home remedies/ traditional medicine do you use?

Home remedies	**Ever used it**		**Still use it**	**How often**		
	Yes	No	Yes	Once a week	Three times a week	More than three times a week
Tulsi leaves						
African potato						
Imbiza						
Mango leaves						
Bitter gourd or karela						
Cinnamon						
Zifozonke						
Fenugreek or methi						

Indian gooseberry or amla						
Impepho						
Black plum						
Curry leaves						
Aloe veera						
Intolwane						
Guava						
Procydin						
Flax seeds						
Neem						
Green tea						
Avocado seeds						
Impinda						
Cloves						
Gambu						
Rosemary or thyme						
Isivumpampuzi						
Drumstick leaves or moringa						
Okra						
Ginger						

Galic						
Lemon and honey						
Zandu						
Weed or marijuana						
Water						
Other: please specify						

Please answer Question 3, 4 and 5 **only** if you **do not use home remedies/ traditional medicine**, thereafter, proceed to section C.

3. Have you been using these home remedies and stopped using it?

Yes ☐ or No ☐

4. If yes, why? _____

5. What are your reasons for not using home remedies/ traditional medicine at all? Please remember you can tick more than one option

A) Do not believe in it ☐

B) The doctor did not tell you to use it ☐

C) Afraid that it will make you more sick ☐

D) Never heard of it ☐

E) Expensive ☐

F) Other ☐

If other, please specify: _____

6. Would you consider using home remedies/ traditional medicine in the future?

Yes ☐ No ☐ Not sure ☐

SECTION C: COMPLICATIONS/ CO-MOBIDITIES OF TYPE 2 DIABETES MELLITUS

1. Do you ever experience any of the following health problems?

Implications/ Co-morbidities	Before diabetes diagnosis		After diabetes diagnosis		How often				
	Yes	No	Yes	No	Very often	Often	Seldom	Very seldom	Don't know
Oral conditions									
Tooth decay and infection									
Loosening of teeth									
Swollen bleeding gums									
Dry mouth									
Cardiac and respiratory problems									
High blood pressure									
Chest pain									
Heart attack									
Neuropathy, muscular and joint related problems									

Arthritis or joint pain									
Coldness of feet									
Numbness of hands									
Numbness of feet									
Cramps									
Dizziness									
Vision difficulty									
Problem in sleep cycle									
Other miscellaneous problems									
Depression									
Weight gain									
Swelling in legs and feet									
Swelling in abdomen									
Hair loss									
Slow wound healing									

Varicose veins									
Anaemia									
Ulcers in the foot									
Other, please specify:									

2. Did you have any amputation?

Yes ☐ or No ☐

If yes, please specify:

_____

_____

3. If yes to Question 2, how long did it take to heal?

_____

4. Do you do the following self-care activities?

Self-care activities	**Yes**	**No**	**How often**				
			Very often	**often**	**seldom**	**Very seldom**	**Don't know**
Follow a healthy diet							

Eat five or more servings of fruit and vegetables a day							
Eat foods high in fat (Avocado, fish, nuts, cheese, etc)							
Eat sweets (chocolates, cakes, biscuits, etc)							
Exercise for at least 30 minutes a day (walking, swimming, etc)							
Check sugar levels regularly							
Take the medication given by the doctor regularly (as prescribed)							
Take the exact number of tablets that is prescribed by doctor							

Thank you for your time!!!

Annexure I: Questionnaire for objective 2 and 3

TRADITIONAL MEDICINE USE AND CO-MORBIDITIES AMONG TYPE 2 DIABETES MELLITUS OUTPATIENTS - A CROSS SECTIONAL HOSPITAL BASED SURVEY IN KWAZULU-NATAL

Imiyalelo yophendulayo:

- Phendula imibuzo engezansi ngepeni elimnyama noma elikuhlaza olinikiwe.
- Imibuzo iphendulwa ngoku faka u "✔" maqondana nebhokisi elinempendulo efanele.
- Uma wenze, iphutha faka isiphambano (ngobunono) bese ufaka u "✔" ebhokisini okuyilo obulihlosile.
- Uma ufuna ukuchaza kafushane maqondana nombuzo, bhala esikhaleni osinikiwe sokuchaza.
- Ucelwa ukuthi uphendule yonke imibuzo elapha ngokuthembeka nangokolwazi lakho oluphelele. Ulwazi luqoqelwa ukuxwayisa abantu ngesifo sikashukela esibhedlela.

Ukugcwalisa lemibuzo akuphoqelekile, futhi imininingwane yophendulayo izoba imfihlo.

SECTION A: DEMOGRAPHICS

1. Ubulili:

Owesilisa ☐ Owesifazane ☐ Okunye ☐

2. Uneminyaka emingaki? _____

3. Ibala: _____

4. Ezenkolo:

Eyamahindu ☐ EyaMasulumane ☐ Eyobukhristu ☐ Ezinye ☐

Uma ukhethe ezinye, zibhale lapha: _____

5. Ezemfundo:

Awukaze uye esikoleni ☐ Amabanga aphansi ☐ Amabanga 8-12 ☐

Usenyuvesi ☐ Usuphothule ☐

6. Umsebenzi?

Emaplazini ☐ Umsizi wasekhaya ☐ uNksz. Ohlala ekhaya ☐

Angisebenzi ☐ Ezitolo ☐ Umhlalaphansi ☐ Okunye ☐

Uma ukhethe okunye, bhala lapha:

_____

7. Imali isiyonke engena ekhaya njalo ngenyanga:

R 0 – R2000 ☐ R2001 – R4000 ☐ R4001 – R6000 ☐ > R6000 ☐

8. Ngumuphi unyaka owathola ukuthi unesifo soshukela emzimbeni wakho? _____

9. Bakhona yini abake baba nenkinga kashukela ngaphambili emndenini wakho?

Yebo ☐ Cha ☐ Angazi ☐

Uma bekhona, isho ubudlelwano (umama, ubaba, udadewethu, umfowethu kanjalo kanjalo) kuleli tafula elingezansi kanye nezinye izinkinga zezempilo abanazo noma ababenazo.

Ubudlwelano bakho naye	**Inkinga yezempilo anayo (ubale noshukela)**

10. Ukulapha isifo soshukela:

Imishanguzo/imithi yodwa ☐ Ukudla ngendlela ☐ Ukudla ngendlela nemishanguzo ☐ Ukudla ngendlela nokuzivocavoca ☐ Ukudla ngendlela, imishanguzo kanye nokuzivocavoca ☐

11. Uhlelo lokulashwa kwakho esibhedlela lume kanjani?

Kanye nge viki ☐ Kabili ngeviki ☐ Kanye ngenyanga ☐

Kabili ngenyanga ☐ Okunye ☐

Uma ukhethe okunye, chaza lapha: _____

SECTION B: Ukusetshenziswa kwamakhambi esintu

1. Uyazisebenzisa ezinye izindlela zokulapha ushukela ngaphandle kwalezi zasesibhedlela?

   Yebo ☐ noma Cha ☐

Uma uthe Yebo, phendula umbuzo 2, uma usuwuphendulile qhubeka nelandelayo weqe umbuzo 3.

Uma uthe cha, weqe umbuzo 2 bese uqhubekela ku mbuzo 3, uma usuwuqedile qhubekela ku Section C

2. Imaphi amakhambi owasebenzisile?

Amakhambi asekhaya	**Asebenzisiwe**		**Kangaki**		
	Yebo	Cha	Kanye ngeviki	Kathathu ngeviki	Kudlule kathathu ngeviki
Tulsi leaves					
Amazambane					
Imbiza					
Amahlamvu kamango					
Bitter gourd or karela					
Cinnamon					
Zifozonke					
Fenugreek or methi					
Indian gooseberry or amla					

Impepho					
Black plum					
Curry leaves					
Inhlaba					
Intolwane					
Guava					
Procydin					
Flax seeds					
Neem					
Green tea					
Izinhlambu zakotapeya					
Impinda					
Cloves					
Gambu					
Rosemary or thyme					
Isivumpampuzi					
Drumstick leaves or moringa					
Okra					
Ginger					
Galic					
Lemon and honey					

Zandu					
Insangu					
Amanzi					
Okunye: chaza					

Phendula umbuzo 3 no 4 uma ungawasebenzisi amakhambi esintu, uma usuqedile, qhubekela ku section C.

3. Yisiphi isizathu esenza ungasebenzisi amakhambi esintu? Ungakhetha noma amangaki amabhokisi, ahambisana nawe

A) Awukholelwa kuwo ☐

B) Akaze udokotela athi ngiwasebenzise ☐

C) Usaba ukuthi angase akugulise kakhulu ☐

D) Akaze wezwa ngawe ☐

E) Ayabiza ☐

F) Okunye ☐

Uma ukhethe okunye, chaza lapha: _____

4. Uyazibona usebenzisa amakhambi esintu esikhathini esizayo?

Yebo ☐ Cha ☐ Mhlampe ☐ Asikho isiqiniseko ☐

SECTION C: IZINKINGA EZINYE EZIHAMBISANA NOSHUKELA

1. Uke ube noma wake waba nazona lezinkinga ezibhalwe ngezansi?

Izinkinga	**Phambi kokutholaka koshukela**		**Sewutholakele ushukela**		**Kangaki**				
	Yebo	**Cha**	**Yebo**	**Cha**	**Kaningi**	**Njalo**	**Lapho nalapho**	**Akuvamile**	**Angazi**
Zomlomo									
Ukubolelwa izinyo									
Ukuxegelwa izinyo									
Izinsini ezivuvukele noma eziphuma igazi									
Umlomo owomile									
Ubuhlungu bamazinyo, uma uhlafuna									

izinkinga ezihlangene nokuphefumula nenhliziyo									
I high high									
Ubuhlungu besifuba									
Ukumelwa inhliziyo									
Ukuphelelwa umoya									
Ukukhwehlela									
Ukuminyana									
Izinkinga ezihlangene nemithambo, imisipha namathambo									
Ukuqina kwemisipha									
Ubuhlungu emajoyintini									
Ukubandelwa zinyawo									
Ukudumba kwezandla nezinyawo									
Amajaqamba									
Isiyezi									

Vertigo									
Ukuzwa									
Ukubona									
Ubunzima bokulala ebusuku									
Ezinye izinkinga ezixubile									
Ukuphazamiseka emoyeni									
Ukukhuluphala									
Ukuvuvukala kwezandla, izinyawo kanye nesisu									
Ukuqothukelwa izinywele									
Inkinga sesikhumba									
Uzilonda ezingapholi									
Varicose veins									
Ukushodelwa igazi									
Ukukhathala									

Hypoglycaemic attacks									
Ulcers									
Ukususwa kwezitho emzimbeni									
Hypertension									
Okunye, chaza:									

2. Uyayenza imisebenzi yokuzinakekela?

Imisebenzi yokuzinakekela	**Yebo**	**Cha**	**How often**				
			Njalo	**Njalo kodwa ayi kaningi**	**Lapho nalapho**	**Makwenzekile**	**Angazi**
Ulandela indlela yokudla ukudla okunempilo							
Udla izithelo nemifino kawu-5 ngosuku							

Udla ukudla okunamafutha							
Udla oswidi							
Ukuzivocavoca ngosuku imizuzu engamashumi amathathu (ukuhamba, ukubhukuda, etc)							
Ubheka ushukela wakho njalo							
Uthatha imithi onikezwe udokotela njalo							
Uthatha amaphilisi onikezwe udokotela ngendlela akuchazele ngayo							

SIYABONGA ISIKHATHI SAKHO!!!

Annexure I (Part 2): HOME REMEDIES/ TRADITIONAL MEDICINE

Study ID.: _____

Name of home remedy: _____

7. How long have you been using this home remedy/ traditional medicine (TM)?

1 year ☐ 2- 3 years ☐ 3- 5 years ☐ more than 5 years ☐

8. How often do you use this home remedy/ TM?

Once a day ☐ Twice a day ☐ 3 times or more a day ☐

Once a month ☐ Less frequent ☐ Other ☐

If other, please specify: _____

9. Why do you use this home remedy? You can tick more than one option

A) Controls my high blood sugar levels ☐

B) I experience less side effects than my tablets ☐

C) I do not have other health problems ☐

C) cheap ☐

10. Do you use it when your blood sugar levels go high?

Yes ☐ or No ☐

11. Do you use it when your blood sugar levels go low?

Yes ☐ or No ☐

12. Do you use this home remedy/TM for treatment of other health problems as well?

Yes ☐ or No ☐

If yes, please specify: _____

13. What type of medication do you get from the hospital for high blood sugar levels?

Tablets ☐ Injections ☐ Other ☐

If other, please specify: _____

14. Are you happy with the medication given to you in hospital?

Yes ☐ or No ☐

15. Do you stop taking your hospital medication when you use this home remedy/ TM?

Yes ☐ No ☐ Sometimes ☐

16. Do you use the home remedy/ TM in conjunction with your hospital medication?

Yes ☐ or No ☐

17. Where did you receive your information about this home remedy/ TM that you use?

Doctor ☐ Pharmacy ☐ magazine ☐ Tv ☐

Nurses ☐ Family ☐ Friends ☐ People waiting in the queue ☐

Radio ☐ Internet ☐

18. Do you feel relief from using this home remedy/ TM?

Yes ☐ No ☐ Not sure ☐

19. Would you tell other sugar patients about this home remedy/ TM?

Yes ☐ No ☐ Not sure ☐

AMAKHAMBI ASEKHAYA/ESINTU

Inombolo yokufunda: _____

Igama lekhambi: _____

1. Sekuphele isikhathi esingakanani usebenzisa leli khambi?

Unyaka owodwa ☐ Iminyaka emibili kuya kwemithathu ☐ Emithathu kuya kwemihlanu ☐ Iminyaka engaphezulu kwemihlanu ☐

2. Ulisebenzisa kangakanani leli khambi?

Kanye ngosuku ☐ Kabili ngosuku ☐ Kathathu nangaphezulu ngosuku ☐

Kanye ngenyanga ☐ Akuvamile ☐ Okunye ☐

Uma ukhethe okunye, chaza: _____

3. Yindaba usebenzisa lelikhambi? Ungakhetha noma kangaki

G) Lilawula amazinga ashukela emzimbeni ☐

H) Zincane izinkinga kunalezi ezifika namaphilisi ☐

I) Azikho ezinye izinkinga zempilo enginazo ☐

C) Ishibhile ☐

4. Uyalisebenzisa uma ushukela wenyukile?

Yebo ☐ Cha ☐

5. Uyalisebenzisa ikhambi lakho uma ushukela uphansi?

Yebo ☐ Cha ☐

6. Uyalisebenzisa leli khambi ukulapha ezinye izinto ngaphandle koshukela?

Yebo ☐ Cha ☐

Uma uthe yebo, chaza izifo ozilaphayo: _____

7. Ikuphi ukulashwa okuthola esbhedlela uma ushukela unyukile?

Amaphilisi ☐ Umjovo ☐ Okunye ☐

Uma ukhethe okunye, chaza: _____

8. Weneme ngemishanguzo/ ngemithi oyithola esbhedlela?

Yebo ☐ Cha ☐

9. Uyayeka ukuthatha imishanguzo/ imithi yasesibhedlela uma uthatha amakhambi akho asekhaya?

Yebo ☐ Cha ☐ Kwezinye izikhathi ☐

10. Uma ucabanga liphephile lelikhambi lesintu uma ulisebenzisa kanye nemithi onikezwe yona esibhedlela?

Yebo ☐ Cha ☐

11. Uma ucabanga ikhambi lakho liphephile kunalemishanguzo/ imithi oyithola esbhedlela?

Yebo ☐ Cha ☐

12. Kuvunyeliwe yini ukusebenzisa lelikhambi enkolweni yakho?

Yebo ☐ Cha ☐

13. Kukhona yini okwenzakalayo uma ungalandelanga imiyalelo yokuthatha ikhamba lakho?

Yebo ☐ Cha ☐

14. Walitholaphi ulwazi ngalelikhambi lakho?

Kudokotela ☐ Ekhemisi ☐ Ebhukwini ☐ KuTv ☐

Kumhlengikazi ☐ Ekhaya ☐ Kubangani ☐ Kolayini ☐

15. Ulindele miphi imiphumela kuleli khambi olisebenzisayo? Ungakhetha noma okungaki.

A) Ukunciphisa ubuhlungu ☐ B) Ukuzigcina ngiphilile ☐

C) Ukulapha ezinye izifo ☐ D) Ukuzithokozisa ☐

E) Ukusebenzisa imishanguzo encane ☐ F) Okunye ☐

Mawukhethe okunye, chaza _____

16. Uyakuzwa ukululama uma usebenzisa lelikhambi?

Yebo ☐ Cha ☐ Angazi ☐

17. Ungalisebenzisa leli khambi futhi?

Yebo ☐ Cha ☐ Angazi ☐

18. Ungabatshela abanye abanenkinga kashukela ngalelikhambi?

Yebo ☐ Cha ☐ Angazi ☐

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Demographic stratification of Type 2 diabetes and comorbidities in district healthcare in KwaZulu-Natal

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Background: Diabetes has been reported as the second leading cause of death and the top leading cause of death amongst women in South Africa; it is important to evaluate any epidemiological or demographic transition related to diabetes. This study evaluated the demographically stratified prevalence of type 2 diabetes mellitus (T2DM) and existing comorbidities amongst an outpatient population in a district healthcare facility in Kwazulu-Natal (KZN).

Methods: This retrospective cross-sectional study was conducted at a district hospital, and a retrospective record review of all outpatients who reported to the hospital to be treated for T2DM between the period, August 2018–January 2019, was used. Data, such as age, sex, ethnicity and any coexisting morbidity, were collected from outpatient hospital registers and electronically captured using a record review tool.

Results: There were significantly more female patients (3072) compared to male patients (1050) ($p < 0.001$) with a mean age of 59.21 years. Hypertension (77.9%) and cardiovascular problems (11.16%) were most frequent. Approximately 84% of women presented with T2DM and either one or two morbidities simultaneously. Female patients were at significantly higher risk of presenting with hypertension (odds ratio [OR] = 1.44, 95% confidence interval [CI]: 1.20;1.71), whilst their risk for cardiovascular problems was significantly lower compared to male patients (OR = 0.67, 95% CI: 0.54;0.83).

Conclusion: The prevalence of T2DM and comorbidities differed by demographic factors, such as sex, ethnicity and age. There is a need for flexible and adaptive approaches for the prevention and management of T2DM cases in order to allocate medical resources efficiently and according to the true burden of disease because of T2DM complications.

Keywords: type 2 diabetes mellitus; demographics; comorbidities; prevalence; healthcare; non-communicable diseases; epidemiology; disease burden.

Background

The International Diabetes Federation (IDF) estimates that 693 million adults will be living with diabetes mellitus (DM) by 2045.[1] It is predicted that by 2030, developing countries will experience as much as a 69% increase in new diagnoses.[2] South Africa (SA) is particularly vulnerable to this epidemic given the increase in urbanisation, prevalence of obesity and physical inactivity and the strained healthcare system already burdened by communicable diseases, such as human immunodeficiency virus (HIV) and tuberculosis (TB).[3] It is imperative to continue tracking both the prevalence and incidence of type 2 diabetes mellitus (T2DM), given the impact on healthcare resources and the implications for the emerging SA National Health Insurance (NHI) policy. Type 2 diabetes mellitus was reported to be the fifth leading cause of death in 2012–2013 (4.4% – 4.8%) and was ranked as the second leading cause of death for women.[4] Barely 2 years later (2015–2016), it is the overall second leading cause of death (5.4% – 5.6%) and ranked as the top leading cause of death amongst women (7.2%).[4] District Health Information System (DHIS) data showed that the provincial crude prevalence of T2DM in KwaZulu-Natal (KZN) was 12.5% which increased to 34.1% when patients with private medical aid and undiagnosed T2DM were considered.[5] Risk factors linked to T2DM are extensively reported.[6,7] However, it is important to evaluate any demographic transition related to T2DM, particularly for mitigation and management.

In SA, there was a 5.5% increase in the prevalence of T2DM amongst people aged 30 years and older between 2000 and 2012.[8] Likewise, in Africa, the prevalence is increased amongst people aged between 40 and 60 years in contrast to those older than 60 years.[9] Sub-Saharan African (SSA) studies demonstrated a peak prevalence in the oldest age group (> 65 years),[10,11,12] in contrast to others who showed a peak prevalence in the 45–64 years age group.[13,14,15] From global estimates, it is likely that the male excess previously reported for SSA is likely to increase by 2025.[16] However, it is evident from available data that the gender distribution varies between and within populations with no obvious trend.[17] Ethnicity and genetic history have been reported as a significant risk factor in T2DM.[18] Asians are reported to have an increased susceptibility for T2DM,[19] which may be similar for SA Indians. Moreover, this T2DM incidence may be increasing amongst Africans as a result of increasing urbanisation and socio-economic conditions coupled with poor nutritional choices.[9] An evaluation of demographic data associated with the incidence and prevalence of T2DM is essential in advancing the precision in the prediction of incidence, complications, mortality and frequency of atypical variants.[20]

Previous studies suggest that chronic complications presented with T2DM reduce the quality of life, increase diabetes-related mortality and pose a significant healthcare burden.[21,22] The spectrum of various comorbidities linked with T2DM requires correct management and is critical in African countries, including South Africa, where limited healthcare resources require strategic allocation. T2DM-related comorbidities include micro- or macro-vascular complications, such as cardiovascular diseases, blindness, peripheral neuropathy and kidney disease,[23] which subsequently increases the risk of strokes, heart attacks and amputations.[24] Other conditions include adverse oral health, arthritis, vision-related issues, depression, slow wound healing, fatigue and hypoglycaemic episodes.[25] Diabetics may present with several of the above conditions simultaneously, contributing to increased mortality and morbidity.[23,26] In addition, demographic factors, such as age, sex and ethnicity, should be considered in relation to comorbidities, given that South Africa is facing an increased burden of non-communicable diseases.[27] KwaZulu-Natal has the largest population of Indians and the highest reported HIV and TB prevalence in SA,[5] predisposing them to increased susceptibility. This study included a retrospective assessment of patients who attended a regional hospital in the EThekwini district (KZN, SA), with the aim of determining the demographic prevalence of T2DM and existing comorbidities.

Methods and materials

Study design and site

This retrospective study was conducted at a district hospital located in the eThekwini health district. The hospital has a catchment population of over 1 500 000 people who are amongst the poorest in the eThekwini district. The hospital has approximately 36 000 admissions in a year, and 600 000 outpatients are treated annually.[28] It serves a population of approximately 240 000.

Study population and sampling strategy

All outpatients who were treated for T2DM between the period August 2018 and January 2019 were included in the study. Permission was sought from the Department of Health and hospital management to conduct the study. Once permission was received, a retrospective review on hospital registers for the 6-month period was carried out to determine the prevalence of T2DM. Data, such as age, gender and ethnicity, were collected and electronically captured using a data capturing tool.

Inclusion criteria

All participants who were:

- treated with T2DM within the 6 months (Aug 2018 – Jan 2019) under study
- reported to R.K. Khan Hospital for chronic treatment for T2DM.

Exclusion criteria

- Type 1 diabetes
- Gestational diabetes

Data collection

A retrospective record review of all outpatients who attended the DM clinic in the hospital for chronic treatment between the period August 2018 and January 2019 was conducted. Data, such as age, sex, ethnicity and any coexisting morbidity, were collected from outpatient hospital registers (paper-based) for a period of 6 months and electronically captured using a record review tool. Data were limited by the information available in the hospital register; demographic variables such as gender, age and ethnicity were available. Clinical data included a record of specific comorbidities such as hypertension, cardiac problems, epilepsy, asthma, arthritis, anaemia and mental health. Cardiovascular problems included congenital heart disease, coronary artery disease, heart failure, heart attack, heart valve disease, cardiomyopathy, atherosclerosis and ischemic heart disease. However, clinical data for other related T2DM-associated morbidities (e.g. oral, ocular and foot ulcers) were not available from the outpatient registers.

Data analysis

Data were captured using Microsoft Excel using double entry procedures, cleaned through range checking and spot checking and coded for data analysis. Data were analysed using STATA version 12 (Statacorp). Descriptive statistics included frequency counts, percentages, mean and standard deviation. T2DM cases from the hospital register were stratified by ethnicity, age and gender to determine

the demographic profile. A test of proportions was used to evaluate differences between demographic variables and sex. Patients with early onset DM were defined as those patients who were first diagnosed with DM before 45 years old. Age was dichotomised by sex, ethnicity and pre-existing comorbidities as both a continuous and categorical variable. The *t*-test was used for comparison of age stratified by sex and pre-existing comorbidities, whilst the chi-squared test of proportions was used to compare T2DM stratified by sex, ethnicity, age and comorbidities. A variable was created to represent the total number of pre-existing comorbidities for each patient as reflected in the hospital register. Multivariate logistic regression models, adjusted for age, were run using the comorbidity as the dependent variable and gender and ethnicity as the independent variables. In addition, we used the frequency of pre-existing comorbidities as a dependent variable with sex and ethnicity as the independent variables. A 95% confidence interval (CI) was reported and $p \leq 0.05$ was considered statistically significant.

Ethical considerations

The study was approved by the Durban University of Technology Institutional Research Ethics Committee (IREC) (REC 112/19) and the KwaZulu-Natal Department of Health.

Results

A total of 4122 (*N*) outpatients were presented with T2 DM between August 2018 and January 2019 at the district hospital. There were significantly more female patients (3072) compared to male patients (1050) ($p < 0.001$) with a mean age of 59.21 years (Table 1). Overall, approximately 10% of patients were presented with early onset DM (< 45 years old), affecting significantly more women than men (309 vs. 132). Most of the new cases presenting with T2DM over the 6-month period were between 55 years and 64 years old (31.59%) with 77.42% of all outpatients between the ages of 45 years and 74 years (Table 1). Diabetic outpatients seeking treatment at the hospital dropped from 644 in August 2018 to 584 in September 2018. A marked increase was noted between October (834) and November (1222), with fewer patients in December (408) and January (429). This reduction may be related to the poor access during the holiday season.

A total of 1514 (36.73%) African and 2493 (60.48%) Indian (South Asian) patients were included for further demographic stratification (Table 2). There was comparatively fewer mixed race and white (Caucasians) patients compared to African and Indian patients (South Asian), so they were excluded from further bivariate and multivariate analysis. Because of low numbers, mixed race and white patients were excluded from further analysis. Significantly, more Indian female patients were presented with T2DM compared with African female patients ($p < 0.05$). Similarly, more Indians were presented with T2DM in each age category compared to Africans. However, the early onset of T2DM was similar between African and Indian patients (214 and 215, respectively).

The categorised prevalence of comorbidities is presented in Table 3. Hypertension (3212) and cardiovascular problems (460) were most frequent, with a prevalence of 77.9% and 11.16%, respectively. Approximately 40% (176/441) of patients with early onset DM also suffered with hypertension. The prevalence of comorbidities, such as hypertension, arthritis and anaemia, was significantly higher amongst female patients than in male patients. Whilst cardiovascular problems were significantly higher for Indians compared to Africans (67% vs. 28%, $p < 0.05$), the converse was true for epilepsy and mental health. The likelihood of presenting with comorbidities increased significantly with age, as most patients aged between 55 and 74 years presented with hypertension, cardiovascular problems and arthritis ($p < 0.05$).

TABLE 1: Age profile of type 2 diabetes mellitus patients presenting at the district hospital stratified by sex.

Demographic	Total		Male		Female		*p**
	n	%	*n*	%	*n*	%	
Total	4122	100.00	1050	25.47	3072	74.53	< 0.005
Age (mean, SD)	59.21	12.84	57.92	12.68	59.66	12.86	0.245
Early onset DM†	441	10.70	132	12.57	309	10.06	0.012
Age category (years)							
0–15	15	0.36	4	0.38	11	0.36	0.016
15–24	44	1.07	14	1.33	30	0.98	< 0.005
25–34	98	2.38	27	2.57	71	2.31	< 0.005
35–44	284	6.89	87	8.29	197	6.41	< 0.005
45–54	972	23.58	266	25.33	706	22.98	< 0.005
55–64	1302	31.59	345	32.86	957	31.15	< 0.005
65–74	917	22.25	209	19.90	708	23.05	< 0.005
75–84	451	10.94	92	8.76	359	11.69	< 0.005
85–98	39	0.95	6	0.57	33	1.07	< 0.005

N = 4122.

SD, standard deviation; DM, diabetes mellitus.

*, $p < 0.05$ was considered statistically significant.

†, Early onset DM includes all patients who were first diagnosed with diabetes when they were < 45 years old.

TABLE 2: Ethnicity-stratified demographic characterisation of all patients with type 2 diabetes mellitus.

Demographic	African		Indian		Mixed race		White	
	n	%	*n*	%	*n*	%	*n*	%
Sex								
Male	345	32.86	671	63.90	6	0.57	28	2.67
Female	1169	38.05	1822	59.31	18	0.59	63	2.05
Early onset T2DM†	214	14.13	213	8.54	2	8.33	12	13.19
Age category (years)								
0–15	9	60.00	6	40.00	0	-	0	-
16–24	31	70.45	12	27.27	1	2.27	0	-
25–34	46	46.94	49	50.00	0	-	3	3.06
35–44	128	45.07	146	51.41	1	0.35	9	3.17
45–54	373	38.37	584	60.08	4	0.41	11	1.13
55–64	541	41.55	721	55.38	11	0.84	29	2.23
65–74	267	29.12	617	67.28	5	0.55	28	3.05
75–84	109	24.17	330	73.17	2	0.44	10	2.22
85–98	10	25.64	28	71.79	0	-	1	2.56

N = 4122.

T2DM, type 2 diabetes mellitus.

†, Early onset DM includes all patients who were first diagnosed with diabetes when they were < 45 years old.

TABLE 3: Existing comorbidities amongst patients with type 2 diabetes mellitus.

Comorbidities	Hypertension		Cardiac		Epilepsy		Asthma		Arthritis		Anaemia		Mental health		TB	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Total	3212	77.92	460	11.16	99	2.40	207	5.02	245	5.94	118	2.86	116	2.81	59	1.43
Sex																
Male	761	23.69	313	68.04	30	30.30	48	23.19	33	13.47	15	12.71	33	28.45	12	20.34
Female	2451	76.31	147	31.96	69	69.70	159	76.81	212	86.53	103	87.29	83	71.55	47	79.66
*p**	< 0.005	-	< 0.001	-	0.264	-	0.439	-	< 0.005	-	< 0.001	-	0.456	-	0.362	-
Race																
African	1149	35.77	130	28.26	53	53.54	46	22.22	107	43.67	36	30.51	53	45.69	27	45.76
Indian	1976	61.52	309	67.17	43	43.43	151	72.95	134	54.69	82	69.49	55	47.41	31	52.54
*p**	0.085	-	< 0.005	-	< 0.004	-	< 0.005	-	0.105	-	0.098	-	< 0.004	-	0.208	-
Early onset DM	176	40.00	21	4.76	8	1.81	24	5.44	9	2.04	10	2.27	8	1.81	3	0.68
Age category (years)																
0–15	1	0.03	1	0.22	-	-	-	-	-	-	-	-	-	-	-	-
15–24	9	0.28	1	0.22	-	-	-	-	-	-	-	-	3	2.59	-	-
25–34	30	0.93	2	0.43	-	-	3	1.45	-	-	3	2.54	1	0.86	-	-
35–44	136	4.23	17	3.70	8	8.08	21	10.14	9	3.67	7	5.93	4	3.45	3	5.08
45–54	710	22.10	90	19.57	26	26.26	53	25.60	55	22.45	30	25.42	30	25.86	17	28.81
55–64	1090	33.94	137	29.78	43	43.43	67	32.37	103	42.04	27	22.88	35	30.17	24	40.68
65–74	799	24.88	141	30.65	10	10.10	44	21.26	52	21.22	35	29.66	27	23.28	8	13.56
75–84	405	12.61	68	14.78	11	11.11	17	8.21	26	10.61	14	11.86	16	13.79	7	11.86
85–100	32	1.00	3	0.65	1	1.01	2	0.97	-	-	2	1.69	-	-	-	-
p	< 0.005	-	< 0.005	-	< 0.048	-	0.321	-	< 0.001	-	0.358	-	0.374	-	0.487	-

N = 4007.

DM, diabetes mellitus; TB, tuberculosis.

*, $p < 0.05$ was considered statistically significant.

When logistic regression was applied using sex and ethnicity (African and Indian) as independent variables, female patients with T2DM were at significantly higher risk of presenting with hypertension (odds ratio [OR] = 1.44, 95% CI:1.20;1.71), arthritis (OR = 2.20, 95% CI:1.51;3.20) and anaemia (OR = 2.42, 95% CI:1.40;4.19), whilst their risk for cardiovascular problems was significantly lower compared to male patients (OR = 0.67, 95% CI: 0.54;0.83). Age-adjusted regression also illustrated a higher risk for cardiovascular problems and asthma amongst Indians with T2DM, with a lower risk for epilepsy, arthritis, and mental health-related problems compared to Africans (Table 4). Table 5 illustrates the number of co-existing morbidities stratified by gender, ethnicity and age. Overall, only 621 (15%) patients had no comorbidity, whilst 2522 (61%) patients suffered at least one diagnosed condition. Hospital registers demonstrated more comorbidities for women compared to men ($p < 0.05$), with 84% (2574/3072) women presenting with T2DM and either 1 or 2 morbidities simultaneously. For both sexes, it was observed that DM plus one comorbidity was the most common combination. Indians presented with significantly more comorbidities than Africans. When the presence of multiple morbidities was further stratified by sex, significantly more Indian male patients presented with DM + 1 morbidity compared to African male patients ($p < 0.005$). Similar results with respect to ethnicity were

TABLE 4: Logistic regression analysis of comorbidities presented by patients with type 2 diabetes mellitus.

Existing comorbidity	Female		Indian		*p*
	OR	95% CI	OR	95% CI	
Hypertension	1.44	1.20;1.71	1.01	0.85;1.20	< 0.005
Cardiac	0.67	0.54;0.83	1.35	1.09;1.68	< 0.001
Epilepsy	0.76	0.48;1.18	0.48	0.32;0.73	0.264
Asthma	1.15	0.82;1.62	2.11	1.50;2.96	0.439
Arthritis	2.20	1.51;3.20	0.77	0.59;0.10	< 0.005
Anaemia	2.42	1.40;4.19	1.44	0.97;2.14	< 0.001
Mental health	0.82	0.54;1.25	0.62	0.42;0.90	0.456
TB	1.28	0.68;2.43	0.70	0.42;1.18	0.362

Note: Models were adjusted for age. Male patients and African patients were the reference categories.

N = 4022.

TB, tuberculosis; OR, odds ratio; 95% CI, 95% confidence interval.

*, $p < 0.001$; **, $p < 0.05$.

TABLE 5: Type 2 diabetes mellitus patients stratified by frequency of comorbidities.

Demographics	Frequency of co-existing morbidities									
	DM only†		DM+1		DM+2		DM+3		DM+4	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Total	621	15.07	2522	61.18	878	21.30	92	2.23	9	0.22
Sex										
Male	208	33.55	605	23.99	221	25.17	16	17.39	-	-
Female	412	66.45	1917	76.01	657	74.83	76	82.61	9	100.00
p	< 0.005	-	< 0.005	-	< 0.005	-	< 0.000	-	< 0.002	-
Race										
African	254	42.12	914	37.17	312	36.84	29	32.95	4	44.44
Indian	349	57.88	1545	62.83	535	63.16	59	67.05	5	55.56
p	< 0.005	-	< 0.005	-	< 0.005	-	< 0.001	-	0.739	-
Early onset DM‡	227	36.55	164	6.50	44	5.01	5	5.43	1	1.11
Age category (years)										
0–15	13	2.10	2	0.08	-	-	-	-	-	-
15–24	32	5.16	11	0.44	-	-	1	1.09	-	-
25–34	62	10.00	30	1.19	4	0.46	1	1.09	-	-
35–44	119	19.19	121	4.80	40	4.56	3	3.26	1	11.11
45–54	170	27.42	597	23.67	187	21.30	15	16.30	3	33.33
55–64	125	20.16	845	33.51	291	33.14	39	42.39	2	22.22
65–74	67	10.81	592	23.47	240	27.33	15	16.30	3	33.33
75–84	28	4.52	294	11.66	112	12.76	17	18.48	-	-
85–98	4	0.65	30	1.19	4	0.46	1	1.09	-	-

N = 4022.

DM, diabetes mellitus.

*, $p < 0.05$ was considered statistically significant.

†, patients presenting with only DM; DM+1: patients presenting with DM and 1 comorbidity; DM+2: patients presenting with DM and 2 comorbidities; DM+3: patients presenting with DM and 3 comorbidities; DM+4: patients presenting with DM and 4 comorbidities

‡, Early onset DM includes all patients under 45 years.

obtained for all other categories of frequency of comorbidities when stratified by sex and age category (Table 6).

Age-adjusted regression analysis was done using sex and ethnicity as independent variables (Table 7). The logit estimate for female patients relative to male patients was significantly lower (β = –0.42, 95% CI: –0.62;–0.21) for presenting with DM only compared to DM + 1 comorbidity ($p < 0.001$), which indicates that male patients are more likely than female patients to present with DM only. None of the other regression analyses using sex and ethnicity were statistically significant.

Discussion

This study demonstrates the demographically stratified prevalence of T2DM and existing comorbidities amongst an outpatient population in a district healthcare facility in KZN. Our data highlight that more women than men present with T2DM and one or more of the existing comorbidities. Even though all reported existing morbidities are not directly linked with T2DM, it impacts on healthcare resources, particularly for treatment modalities. Moreover, this was shown to be significantly influenced by demographic factors such as sex, ethnicity and age. Indians were overrepresented in the population under study, and logistic regression showed a greater risk of disease burden amongst Indians compared to Africans, particularly with respect to hypertension. The high burden of T2DM and hypertension as coexisting morbidities (77.9%) and the 10% prevalence of early onset DM (patients < 45 years) should be noted as serious concerns in an epidemiological transition in SA where non-communicable diseases (NCDs) are increasingly prevalent.

TABLE 6: Demographic profile of type 2 diabetes mellitus patients stratified by frequency of comorbidities.

Demographics	African								Indian							
	DM+1		DM+2		DM+3		DM+4		DM+1		DM+2		DM+3		DM+4	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Sex																
Male	187	31.75*	69	32.39	6	40.00	1	-	402	68.25*	144	67.61	9	60.00	-	-
Female	727	38.88	243	38.33	23	31.51	4	44.44	1143	61.12	391	61.67	50	68.49	5	55.56
Early onset DM†	75	35.05	20	9.35	2	0.93	-	-	83	38.97	23	10.80	3	1.41	1	0.47
Age category (years)																
0–15	2	100.00	-	-	-	-	-	-	-	-	-	-	-	-	-	-
16–24	7	63.64	-	-	-	-	-	-	4	36.36	-	-	1	100.00	-	-
25–34	12	41.38	2	50.00	1	100.00	-	-	17	58.62	2	50.00	-	-	-	-
35–44	54	46.55	18	46.15	1	33.33	-	-	62	53.45	21	53.85	2	66.67	1	100.00
45–54	225	38.59	87	46.52	7	46.69	1	33.33	358	61.41	100	53.48	8	53.33	2	6.67
55–64	354	42.86	117	42.09	15	41.67	2	100.00	472	57.14	161	57.91	21	58.33	-	-
65–74	178	30.96	66	29.07	2	14.29	1	33.33	397	69.04	161	70.93	12	85.71	2	6.67
75–84	74	25.69	22	20.37	3	17.65	-	-	214	74.31	86	79.63	14	82.35	-	-
85–98	8	27.59	-	-	-	-	-	-	21	72.41	4	100.00	1	100.00	-	-

DM only: patients presenting with only DM; DM+1: patients presenting with DM and 1 comorbidity; DM+2: patients presenting with DM and 2 comorbidities; DM+3: patients presenting with DM and 3 comorbidities; DM+4: patients presenting with DM and 4 comorbidities.

$N = 4122$.

DM, diabetes mellitus.

*, $p < 0.001$; **, $p < 0.05$; ***, $p < 0.005$.

†, Early onset DM includes all patients under 45 years.

TABLE 7: Regression analysis of the number of comorbidities (frequency) stratified by sex and ethnicity.

Frequency of comorbidities†	Female		Indian	
	β-coeff	95% CI	β-coeff	95% CI
DM only‡	–0.42*	–0.62;–0.21	0.06	–0.13;0.25
DM+2	–0.07	–0.25;0.10	–0.01	–0.18;0.15
DM+3	0.4	–0.15;0.95	–0.2	–0.28;0.63

Note: Reference categories were male patients and African patients.

DM, diabetes mellitus; 95% CI, 95% confidence interval.

*, $p < 0.001$.

†, The frequency of DM + 1 comorbidity was the base outcome. DM+4 was excluded because of low frequency.

‡, Patients presenting with only DM; DM+1: patients presenting with DM and 1 comorbidity; DM+2: patients presenting with DM and 2 comorbidities; DM+3: patients presenting with DM and 3 comorbidities; DM+4: patients presenting with DM and 4 comorbidities.

T2DM prevalence has been reported in several studies conducted in South Africa;[24,29] however, incidence data have been limited. Despite the recent reporting incidence of DM for 11 districts in KZN by Sahadew et al.,[5] the data are limited in which only DHIS data were used. District Health Information Systems data contain patient visits for T2DM treatment aggregated per healthcare facility and exclude individual patient tracking through identifiers. Thus, it may be possible that a single patient could be counted several times as patients may report to the facility on a monthly basis to collect their medication. This study presents T2DM patients who were given unique hospital identifiers at their first visit for treatment. Moreover, we chose a 6-month period as some diabetics would only see a doctor once every 6 months, whilst continuing to collect their chronic medication at an affiliated clinic.

Our data revealed a significantly higher prevalence of T2DM amongst female patients in contrast to male patients, irrespective of age and sex. This may be associated with sociocultural factors such as varying behavioural patterns between male patients and female patients which influences their nutritional patterns, lifestyle and attitudes towards treatment and prevention.[30] Access to healthcare differs amongst male patients and female patients, as a result of their personal preconceptions.[31] Hi-tech and rapid remedies are usually pursued by men in contrast to the extensive sociocultural therapies pursued by female patients.[31] It is believed that the sociocultural female nature permits an escape from financial and societal drawbacks, whereas the masculine nature of males prompts the search for care that warrants a comprehensive speedy recuperation and lower economic burden.[31] In addition, health-seeking behaviour may be higher for women compared to men in South Africa, particularly with respect to chronic diseases.[32] Hence, it is possible that sociocultural and socioeconomic factors combined with spiritual beliefs and semantics are instrumental in understanding the bolder health-seeking behaviour represented by the higher percentage of women in our sample.

African data for gender distribution in T2DM have reported conflicting results. An increased prevalence amongst male patients was reported from studies in Tunisia, Egypt, Sudan, Cameroon and rural Tanzania,[14,33,34,35] whilst prevalence was greater amongst female patients in South Africa (Durban), Mali, Cameroon and Sudan[14,34,36] with an equal gender distribution reported from South Africa (Cape Town), Tanzania and Sudan.[15,30,36]

Recent reports suggest that diabetics are predisposed to one or more comorbidity.[37] A study conducted in 12 primary healthcare clinics in South Africa revealed a 79% prevalence of hypertension, whilst complications related to the eyes, feet and kidneys were 8.2%, 6.5% and 21.4% respectively.[34] Data on comorbidities-linked to eyes, feet and kidneys were not available for this study as we were limited by the hospital-outpatient register. T2DM is reported as the seventh leading cause for the risk of increased infections, morbidity and mortality in South Africa[24] and accounted for approximately 68 000 deaths in 2013.[5] However, this may be a significant underestimation, when considering the mortality from complications or comorbidity associated with DM. The high prevalence of hypertension (77.9%) amongst patients should be highlighted, particularly that 80% women (2451/3072) and 40% of all early onset diabetics (176/441) presented with hypertension. Our data are in contrast with earlier data from ref. 38, which suggested that hypertension affects 20%–60% of patients with T2DM, depending on obesity, ethnicity and age. It would appear that morbidity associated with hypertension, which is a common complication of T2DM, is increasing. This is of concern as the combination of DM and hypertension increases the risk of premature cardiovascular disease.[38]

Regression analyses demonstrated that female patients with T2DM were at significantly higher risk of presenting with hypertension (OR = 1.44, 95% CI:1.20–1.71, $p < 0.001$) and arthritis but had a lower risk for cardiovascular problems compared to male patients (OR = 0.67, 95% CI: 0.54–0.83, $p < 0.001$). Likewise, the risk of cardiovascular disease (CVD), especially myocardial infarction, was also shown to be greater in a Danish cohort of female diabetic patients below 50 years.[39] More recently, female patients already diagnosed with T2DM develop a greater risk to acquire CVD, with overweight/obesity and postmenopausal women being at a higher risk.[40] We also found that the prevalence of comorbidities was highest amongst Indians regardless of age and sex, in contrast to other race groups. Regression data further demonstrated that Indians with T2DM were predisposed to a higher risk for cardiovascular problems and asthma, but had a lower risk for epilepsy, arthritis and mental health issues compared to Africans. The 12.5% crude prevalence of T2DM in KZN was higher than the 9.2% national prevalence, which could be because of the large population of Indians (South Asian) living in KZN in contrast to other cities in SA, suggestive of a possible genetic predisposition to T2DM.[5,15] Our data suggest that comorbidities increase significantly with age, which is in agreement with the study made by Uddin et al.[41] Uddin and co-workers reported that T2DM + 1 and T2DM + 2 comorbidities were higher in male patients, whilst DM + 3 comorbidities were higher amongst female patients.[41] However, our data showed significantly more female patients with T2DM + 1, T2DM + 2, T2DM + 3 comorbidities ($p < 0.05$), which was suggestive that sex, ethnicity and age are critical determinants associated with the prevalence of T2DM and comorbidities.

Demographic data are essential in advancing the precision in the prediction of incidence, complications, morbidity and mortality related to T2DM.[20] Data obtained from such analyses will accurately inform healthcare systems and enhance the development of tracking proficiencies required for reducing the incidence of DM and associated comorbidities. To date, the management of T2DM following a uniform treatment algorithm is usually associated with poor treatment adherence and the subsequent development of complications.[42] Recent data suggest that some medications may serve dual purposes, for example, the use of metformin (a first line treatment for T2DM) reduced asthma-related outcomes in patients who presented with T2DM and asthma concurrently,[43] whilst hydroxychloroquine (commonly used antirheumatic medication) demonstrated hypoglycaemic effects.[44] The healthcare system in SA, which is already burdened by the HIV/TB epidemic coupled with increasing infectious diseases, could be further constrained by the increasing prevalence of diabetes and comorbidities. Various studies conducted in South Africa, Nigeria, Ghana, Cameroon and Tanzania confirm both the increase in prevalence and the changing epidemiology of diabetes complications;,[17] however, these data are over 15 years old. Arising from these predictions, it is crucial to re-evaluate the extent of the problem so that healthcare resources may be appropriately allocated. In order to gain better control of chronic complications, treatment and management for T2DM and complications, interventions should primarily target the highly prevalent populations with chronic complications including older diabetic patients and those with a long history of diabetes.

A limitation of this study is that as this study was hospital-based, the results only apply for diabetics requiring primary level of healthcare rather than representing the total population of diabetics which include people able to access medical aid and private healthcare. In addition, hospital outpatient records did not include information about microvascular conditions that are a significant comorbidity related to diabetes-linked mortality and morbidity.

Conclusion

The variation of complications with age, gender and ethnicity amongst patients with a T2DM diagnosis all point to a need for flexible and adaptive approaches for the prevention and management of T2DM cases in order to allocate medical resources efficiently and according to the true local burden of disease because of T2DM complications. Findings arising from this study are specific to the Indian and African populations in KZN, but may be aligned with some from other provinces in South Africa. Future research evaluating long-term clinical outcomes in high-risk sub-populations, based on ethnicity, age and underlying comorbid conditions, is warranted for more effective management. Furthermore, the disparities in comorbidities linked with T2DM based on ethnicity warrant the exploration of precision medicine amongst indigenous populations in

South Africa. The use of precision medicine in stratifying diabetics into groups based on the molecular and genetic biomarkers as well as clinical characteristics has been explored to optimise therapeutic outcomes, with the intention of providing recommendations that target groups rather than individual patients. This may be an exploratory option for SA where the increasing prevalence of T2DM, coupled with the attributable burden of associated comorbidity, has the potential to create significant pressure on the healthcare system.

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Competing interests

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Authors' contributions

L.C. was the primary investigator, and N.G., G.M.G. and P.R. conceptualised and supervised the study. All authors contributed to the preparation of this manuscript.

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Data availability

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy of any affiliated agency of the authors.

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