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The association between health related quality of life and some indicators of severity and control in type 2 diabetic patients

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2015-03-27
http://hdl.handle.net/10539/17355

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Chapter 1: INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder of multiple aetiology, characterized by chronic hyperglycaemia, resulting from defects in insulin secretion, insulin action, or both.[1]

The World Health Organisation (WHO) has declared; “The world is facing a growing diabetes epidemic of potentially devastating proportions. Its impact will be felt most severely in developing countries”.[2] According to the WHO, the number of people suffering from DM globally is estimated to be 366 million individuals, and forecast to reach 552 million individuals by 2030. While type 1 and type 2 DM are both increasing, the prevalence of type 2 DM is reported to be increasing at a greater rate. Furthermore, it is estimated by the WHO that approximately 80% of diabetics currently reside in developing countries. [2] While this indicates that the prevalence is greater in these regions, other factors such as age and lifestyle, are reported to be significant precursors to DM, specifically to type 2 DM.

Wild et al has reported that DM increases with age.[3] In 2005, it was found that the prevalence of DM in the United States was estimated to be 0.22% in those less than 20 years of age and 9.6% in those greater than 20 years of age.[2, 3] In individuals greater than 60 years of age, the prevalence of DM was 20.9%. While the prevalence of DM is similar in men and women throughout all age ranges, at the age of 60, men tend to show an increased prevalence in comparison to women. Global estimates forecast that by 2030, the greatest number of individuals with DM will be between 45 and 64 years of age. The most important demographic change to the prevalence of DM, across the world appears to be the increase in the proportion of people greater than 65 years of age.[3]

While the effect of age is widely reported to be a critical factor in DM, lifestyle measures have been further reported to exacerbate the impact of DM.[2, 3] The cause of the increasing prevalence of DM is reported to be the increasing trend towards a sedentary lifestyle: reduced exercise and physical activity; obesity and an unhealthy, unbalanced diet where there is an excess in energy intake over expenditure. Furthermore, an increase in sedentary lifestyle indicates that the proportion of obese individuals is escalating rapidly which may in turn create a burden on the public health systems. Closely related to obesity is an increase in complications related to DM that may be expected.[3]

1.1 Types of DM:

The WHO currently recognises two types of DM, type 1 and type 2 DM; however type 2 is much more prevalent.

The cause of type 1 DM is an absolute deficiency of insulin secretion. Individuals at increased risk of developing type 1 DM can often be identified by serological evidence of an autoimmune process occurring in the pancreatic β islet cells and by genetic markers.[5]

In type 2 DM, the more prevalent type, the cause is mostly a combination of resistance to the action of insulin, supplemented by an inadequate compensatory insulin secretory response which include an abnormal entero-insular axis as well as an abnormal glucagon response.[5] Hyperglycaemia may be present for a sustained period of time prior to the appearance of any clinical signs and symptoms. The underlying hyperglycaemia is sufficient to cause both pathologic and functional changes in various target organs.[5] The present study focused on type 2 DM.

In some individuals with DM, adequate glycaemic control may be achieved with the combination of dietary measures, weight reduction and exercise, and/or oral hypoglycaemic agents (OHA). These particular individuals therefore do not require exogenous insulin. On

the other hand, there are individuals who have some residual insulin secretion left but still require exogenous insulin for adequate glycaemic control. Individuals with extensive β islet cell destruction with subsequently no residual insulin secretion require insulin for survival. The severity of the metabolic abnormality can progress, regress or stagnate. Thus, the degree of hyperglycaemia is a reflection of the severity of the underlying metabolic process and its treatment, more than the nature of the underlying process itself.[5]

The chronic hyperglycaemia of DM is associated with long-term damage and dysfunction in multiple organ systems of the body. The chronic complications can be divided into vascular and nonvascular complications. Vascular disease is a major cause of complications of DM. The vascular complications of DM are further subdivided into microvascular and macrovascular complications.[5]

1.2. Microvascular and Macrovascular complications related to DM

1.2.1 Microvascular disease

Microvascular disease complications include:

- retinopathy with loss of vision
- nephropathy leading to renal failure, dialysis and renal transplant
- peripheral neuropathy, with risk of foot ulcers, amputations, infections including osteomyelitis and Charcot's osteoarthropathy; and
- autonomic neuropathy causing gastrointestinal, genitourinary, cardiovascular symptoms and sexual dysfunction.

1.2.2 Macrovascular disease

Macrovascular disease complications include:

- Coronary artery disease (CAD)
- Peripheral vascular disease (PVD)
- Cerebrovascular disease (CVD)

Both microvascular and macrovascular disease contribute to the high morbidity and mortality rates associated with DM. Atherosclerotic disease occurs with increased frequency in DM, resulting in an increased incidence of myocardial infarction (MI), strokes, claudication and gangrene of the lower limbs. The effects of large vessel disease are devastating in type 2 DM and are responsible for approximately 75% of deaths.[6] Hypertension (HT) and dyslipidaemia are common co-morbid diseases found in patients with DM.

Dyslipidaemia is common in type 2 DM. While poor glycaemic control plays an important role, other factors such as genetic predispositions and/or obesity should not be forgotten.[7] Individuals with DM may have several forms of dyslipidaemia. The most common pattern of dyslipidaemia is hypertriglyceridemia and reduced HDL cholesterol levels.

HT may accelerate other complications of DM, particularly CVD and nephropathy. The Heart Protection Study Collaborative Group, Heart Protection Study, reported that CAD was the foremost cause of death among diabetic patients as a result of dyslipidaemia[8], suggesting that the treatment of dyslipidaemia in patients with type 2 DM, with cardiovascular disease is significantly suboptimal.[8]

PVD is increased in individuals with type 2 DM. The Framingham Heart Study revealed a marked increase in PVD, CAD, MI and sudden death (risk increased from one to five fold) in DM.[9] The American Heart Association (AHA) has described DM as a major risk factor for CVD (same category as smoking, HT and dyslipidaemia). The increase in cardiovascular morbidity and mortality is thought to be caused by the compounding effect of hyperglycaemia with other cardiovascular risk factors.[10]

As evident in the literature quoted above; the impact of DM extends far beyond glycaemic control and target organ damage in patients suffering with DM and has far reaching consequences with regards to the patient's health and lifestyle.

With the above in mind, this study focused on the impact of age, gender, BMI, concurrent HT, dyslipidaemia and glycaemic control (HBA_{1C}) on the health related quality of life (HRQOL) in type 2 DM. In addition, lifestyle measures such as smoking and alcohol consumption were assessed to understand the impact of these variables. While existent literature is sparse on the impact of smoking and alcohol consumption, this study sought out to understand the impact of these lifestyle measures on type 2 DM.

Unlike in acute illnesses, the burden of the management of DM falls largely on the individual living with the condition. Diabetic patients are primarily responsible for their glycaemic control, which is a complex process, requiring not only an understanding of DM but also high levels of character strength and empowerment, a firm belief in one's capabilities, good compliance and a high sense of diligence by performing complex self-care activities daily, and importantly having a supportive environment (of family, friends and health care professionals). Self-care is fundamental to optimising patient's diabetic outcomes which subsequently influences patient's compliance to treatment. Patient's lives are filled with various priorities and the onus remains on the patient as to how much time they will dedicate towards their treatment regimen and their level of compliance.[30]

Long-term complications of DM may only be prevented by a firm, life-long commitment to a treatment regimen.[30] It is crucial that patients recognize this and adhere to their treatment regimen, which allows them an improved HRQOL, thus reducing the morbidity and mortality associated with DM, and ultimately reducing the noteworthy strain on public health care funding.

In addition to diabetes-related complications, fear of and episodes of hypoglycaemia, change in lifestyle and the fear of long term consequences may lead to reduced HRQOL. Individuals with DM, have reduced HRQOL compared to those without DM in the same age group, and their HRQOL decreases with disease progression and complications.[12, 104]

1.3 Health related quality of life

Quality of life (QOL) is described as a multidimensional construct incorporating an individual's subjective perception of physical, emotional, and social well-being, including both a cognitive component (satisfaction) and an emotional component (happiness).[14]

Polonsky reports that, there is currently no "gold standard" for the assessment of overall, health-related, or diabetes-specific QOL.[13]

QOL is also now increasingly being recognised as an important outcome of health, representing the ultimate goal of all health care interventions. The WHO, for the last 50 years, has reported that health is defined not only by the absence of disease and infirmity, but also by the presence of physical, mental, and social well-being.[24]

Rubin and Peyrot provide a comprehensive review of the conceptual and practical issues for assessing QOL in DM. They described three categories of determinants influencing QOL, including medical predictors (e.g. type and duration of DM, treatment regimen, level of glycaemic control, and presence or absence of complications); attitudinal predictors (e.g. self-efficacy, locus of control, and social support); and demographic predictors (e.g. age, gender, education level, ethnicity, and marital status).[14]

The measurement of HRQOL can be defined as the level of health status defined by the individual patient’s perception. It has been stated that because of this bi-dimensionality of HRQOL measurement, that researchers are able to gain insight into and understand the

factors that shape patient's attitude and behaviour towards their disease as well as their ability to adhere to their treatment regimens.[14]

In the study of DM, the earlier QOL literature focused on describing the state of health of individuals with complications, as individuals requiring renal dialysis or kidney transplantation, or those suffering from blindness or foot amputations.[15-20] Furthermore, studies of the psychological impact of DM and its effects on patient's QOL were considered important for understanding the patient's ability to adhere to challenging and demanding treatment regimens.[15]

As with many chronic diseases, diabetic patients are less concerned with clinical biomarkers[16] such as HBA_{1C}, blood pressure, or lipid levels, and are more concerned with how the disease will impact their lives in various domains. These domains include physical and social function, emotional and mental health, burden of the illness, stigma attached to the disease, and how their treatment will impact their daily life.[17] QOL measures, which include many of these domains, may be more meaningful than clinical parameters from the patient's perspective. [18]

Many researchers have questioned the importance of evaluating the HRQOL of patients; however measuring HRQOL in type 2 DM is important as reduced HRQOL may lead to diminished self-care. Diminished self-care then subsequently leads to poor glycaemic control, worsening of symptoms and increased risk for diabetic complications. The dietary restrictions of diabetes, use of medication (OHA or insulin), and the actual symptoms of the disease as well as concomitant diseases, all may also lead to deteriorations in HRQOL. Thus, the evaluation of QOL is fundamental, as it allows health care workers to predict an individual's capability to manage his/her disease and thus to maintain good long-term health care and well-being.[14]

Conventional outcome assessment for DM relies on laboratory indicators, primarily on haemoglobin A1C (HbA_{1C}) and complications of diseases.[25] However, the exclusive reliance

on clinical outcomes, does not necessarily reflect a patient's perception of his/her health. Treatment regimens that require changes in lifestyle and behaviour can influence patients' daily functioning and general well-being. Therefore, HRQOL is increasingly being used as an outcome indicator alongside traditional biomarkers.[25]

In addition to the above, the guidelines for the treatment of type 2 DM emphasize that one of the primary objectives is to improve HRQOL. This may imply that HRQOL should commonly be used as an outcome measure to monitor the burden of DM on the population. The results of previous studies show that HRQOL is associated with the duration of diabetes, age, gender, diabetic complications, co-morbid diseases and the severity of the disease itself.[24]

The benefit of assessing patient's QOL is to provide an individualized personal assessment based on the patient's expectations from the health care worker and thus develop a tailored, effective and realistic treatment regimen best suited to that individual patient. This will promote compliance and reduce complications of the disease and ultimately lead to a better perceived HRQOL.

1.3.1 Instruments to measure HRQOL

Various instruments have been developed to measure HRQOL which either use generic or disease specific instruments. Past research suggests that disease-specific measures may better capture the dimensions of HRQOL most affected by DM, however the disease-specific measures are not designed to capture the deficits associated with co-morbidities, i.e. they are not specific to DM. [26]

Generic instruments are designed to investigate aspects of health that are of universal importance, and allow comparisons of HRQOL amongst different age groups of patients with different chronic diseases. These may be useful for capturing the additional HRQOL deficits associated with co-morbid diseases and their respective treatments, such as HT,

dyslipidaemia and depression, as they incorporate a wider range of dimensions of HRQOL. By contrast, diabetes-specific instruments capture the specific impact that diabetes has on a patient's daily functioning, well-being and subsequently on their QOL; and thus could be more sensitive to small clinically important differences. Reviews have shown that the dimensions covered by diabetes-specific instruments vary, but generally include physical and psychological functioning, social-role fulfilment, diabetes control, and treatment satisfaction.[26]

Amongst the most well-known generic instruments are the Short-Form Health Survey (SF-36) (this is the shortened version of the RAND Corporation's MOS Functioning and Well-being profile)[31], the Quality of Well-being (QWB) scale, its successor, the Quality of Well-being Self-Administered Scale (QWB-SA)[32], and the Euroqol 5D and the COOP/WONCA charts.[31]

The Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) is a commonly used generic instrument for diabetes, while the Diabetes-39 (D-39) has been demonstrated to have good psychometric properties.[25]

In this study, the D-39 questionnaire was used. The D-39 as developed by J. Gregory Boyer and Jo Anne L Earp, is a 39-item instrument that was designed to assess HRQOL for patients with type 1 and type 2 DM. This instrument covers the dimensions of energy and mobility (EM), diabetes control (DC), anxiety and worry (AW), social burden (SB), and sexual functioning (SF). Items are administered using seven response categories, ranging from not affected at all (score = 1) to extremely affected (Score = 7). The subscale scores are calculated by summing responses across all items in the same subscale, with high scores representing poor HRQOL. A summary score is further derived from the five subscale scores of the D-39.[25]

Similar studies using generic instruments to measure QOL include:

- A study done in Canada, Bella Coola valley with regards to HRQOL and type 2 DM showed that having DM is associated with lower HRQOL scores. Factors associated with HRQOL scores include duration of diabetes, insulin use, and diabetes-related complications. Improved glycaemic control, as measured by HbA_{1C} levels, was paradoxically associated with lower HRQOL scores.[27] The study concluded that strategies designed to diagnose diabetes early and aggressively manage blood pressure, dyslipidaemia, and albuminuria may not only prevent diabetes-related complications, but may also prevent irreversible deterioration of HRQOL in diabetic patients.[27]
- A study in Netherlands concluded that diabetes without micro/macrovascular complications had a HRQOL only slightly lower than similar aged persons in the general population. Insulin therapy, obesity and diabetic complications were associated with a lower HRQOL. Higher HbA_{1C} levels did not seem to materially affect the HRQOL.[28]
- A study done in Greece looked at predictors of HRQOL in type 2 DM patients. The study found that the most important predictors of impaired HRQOL were female gender, diabetic complications, non-diabetic co-morbidity and years with DM. Older age, lower education, being unmarried, obesity, HT and dyslipidaemia were also associated with impaired HRQOL in at least one SF-36 subscale and also showed that diabetes-related indicators were more important disease predictors, compared to socio-demographic variables.[29]
- A study done by Khanna et al, in 2012, evaluated the association between HbA_{1C} and diabetes-specific QOL among patients completing diabetes self-management programs. They found that improvements in HbA_{1C} among participants completing a diabetes self-management program were associated with better diabetes-specific QOL.[42]

- A similar study done at a diabetic centre in the private sector in South Africa (SA), found that insulin usage was strongly associated with a lower HRQOL. However the other parameters studied i.e. HbA_{1C}, BMI, exercise and the use of OHA, antihypertensive and dyslipidaemic agents were not found to be strongly associated with HRQOL.[30]

Most of these studies used generic instruments to measure QOL.

Despite an extensive search, no similar study measuring HRQOL in the public sector in SA was found.

1.4 Indicators of severity and control of diabetes

Selected measurements of severity of disease used in the study include:

- Glycosylated haemoglobin (HbA_{1C}) levels. This investigation is extensively used in clinical practice. It is a measure of the blood glucose levels over the previous 3 months and correlates well with the risk of complications. While previously only being used as a marker of chronic glycaemia, the American Diabetes Association (ADA) recommends that HBA_{1C} be used as an assay in the diagnosis of diabetes. According to the Diabetes Care and Control Study (DCCT) data [31], HbA_{1C} levels of less than 7% are desired because they prevent or significantly delay complications of DM.[31]
  The International Diabetes Federation (IDF) and the American College of Endocrinology (ACE) have recommended a HBA_{1C} of less than 6.5%, however there is little evidence to support that aiming for such a low target, will improve cardiovascular outcomes, particularly in patients with long standing DM.[32] On the contrary, as shown in the ACCORD, ADVANCE and VADT studies; aiming for such a low HBA_{1C} in patients with established CAD is associated with increased mortality.
  [109,110,111]

Some studies report a positive association between higher levels of perceived QOL and good glycaemic control, especially when QOL is assessed by disease-specific measures.[12] This was also found in a recent study done in Houston, where Khanna et al, found that lower HBA_{1C} levels were associated with better QOL scores in type 2 DM. [42]

- Body Mass Index (BMI). BMI is a numerical indicator calculated by taking weight in kilograms and dividing it by the height in meters squared expressed as kg/m^2. These ranges of BMI values are valid only as statistical categories. This measure is preferable to absolute weight because it takes the height of the patient into consideration. This measurement has become the standard in clinical practice where weight is being assessed.

  Patients were classified as underweight (BMI $<20kg/m^2$), normal (BMI 20 to $24.9kg/m^2$), overweight (BMI >25 to $29.9kg/m^2$), and obese (BMI $>30kg/m^2$).

  Increased body fat is generally associated with an increase in risk of metabolic diseases such as type 2 DM. A higher incidence or prevalence of DM has been reported to be associated with a high BMI in several previous studies from Asia.[117]

  In this study, the patient's height and weight measurements on the day of the clinic visit were used.

- Exercise: The beneficial effects of exercise have been shown in many studies including "The Harvard Alumni Study" [43] and "The Insulin Resistance Atherosclerosis Study".[44]

  It is recognised that regular physical exercise is important in both the prevention and treatment of type 2 DM with an average reduction of HBA_{1C} of 0.6% The benefits of exercise are many and several mechanisms are involved which include increased

energy expenditure, which when combined with dietary restriction, leads to decreased body fat, increased insulin sensitivity, improved long term glycaemic control, improved lipid profiles, reduced anxiety and stress, lower blood pressure, and increased cardiovascular fitness. The improved insulin-sensitizing effect of exercise is not only restricted to muscle but extends to both hepatic and adipose tissue as well.

A number of cohort studies have demonstrated that in patients with type 2 DM, regular physical activity and moderate to high levels of cardio-respiratory fitness are associated with significant reductions in cardiovascular and overall mortality of 39-70% over a 15-20 year period [32.] Exercise is fundamental in the management of DM. In the diabetic clinic at HJH, at every visit, while awaiting their consultation, patients are seen by the physiotherapist and are encouraged to participate in an exercise routine for 5-10 minutes.

Other variables used in the study:

Studies have shown that HRQOL assessment scores for diabetics are much lower than those reported for non-diabetics [33-40]. The reason for lower scores in patients with DM is most likely multifactorial. Compared with non-diabetics, diabetic patients tend to be older and overweight; are less likely to exercise; are much more likely to have co-morbidities (e.g. HT, CAD, dyslipidaemia); and are more likely to have complications.[33-36, 41] All these factors have been associated with lower HRQOL scores.

- Demographic variables: Some demographic variables are associated with QOL in people with diabetes, just as they are in the general population: Men and younger

individuals generally report better QOL than women and older individuals. Those with higher education or income generally report better QOL than those with less of either. There is evidence that a longer duration of DM is associated with a poorer HRQOL [34, 45-47], but some studies have failed to find this association.[12,48,49]

- Number of insulin units used per day: Patients were asked to quantify their insulin usage per day in the questionnaire. No distinction was made between the various types of insulin in this study or the number of times a patient injected themselves.

  Results of research on the association between treatment regimen and HRQOL in patients with DM are mixed, with some indication that intensifying treatment in patients with type 2 DM from diet and exercise alone, to OHA, to insulin, is associated with worsening HRQOL. Jacobson et al reported that patients taking insulin reported less QOL-assessed satisfaction with treatment and more burden of illness than those taking OHA or none at all.[50] This was also found in a similar study done at a diabetic centre in the private sector in South Africa (SA), where insulin usage was found to be strongly associated with a lower HRQOL.[30]

  However, others have found lower QOL scores in type 2 patients treated with insulin compared to those who were not.[46, 49-50]

- Hypertension (HT): Hypertension is a preventable disease. In many countries, 15% to 30% of the adult population and more than 50% of the elderly population suffer from high blood pressure. There is evidence that antihypertensive treatment significantly decreases cardiovascular morbidity and mortality.

Research has shown that obesity, HT, and DM tend to be linked. Therefore, it is important to understand the effects of having these three diseases, on health and QOL. One study looked at the relationship between having these diseases and the HRQOL for patients who were age 60 and above. The study showed that patients who were solely obese, solely hypertensive, or solely diabetic showed a worse HRQOL on all the scales when compared to those without the three diseases.[53] In men, diabetes was the only factor to be significantly associated with the greatest reduction in HRQOL on most scales, while for women, it was obesity. Women who had all three diseases showed the maximum deterioration in HRQOL across all of the scales, and the deterioration is greater than can be expected from the individual scores for the three diseases combined.[53] This shows that for this type of health rating scale, the negative effects of obesity, HT, and DM on individuals' health are greater than the effects of the three combined.[53]

Another study by Modan et al, with 2,475 subjects, found that 83.4% of the patients with hypertension, were either glucose intolerant (GI) or obese. GI and obesity are both established insulin-resistant conditions. In this study, fasting insulin levels were measured. They found that the mean increment in summed insulin levels (milli-units per litre) in non-obese normotensive patients with normal tolerance was 12 for HT alone, as compared with 47 for obesity alone, 52 for GI alone, and 124 when all three conditions were present. Researchers have found that insulin resistance/ hyperinsulinemia are present in the vast majority of patients with HT, and they constitute a common pathophysiologic feature of obesity, GI, and HT, providing a possible explanation for their common association with eachother.[54]

In studies such as Trials of Hypertension Prevention (TOHP) [55] and Treatment of Mild Hypertension (TOMHS), the decrease in blood pressure was followed by an improvement in the HRQOL.[56] Aydemir et al. showed that hypertensive patients

have a statistically significant decrease in all HRQOL domains as assessed by the SF-36 when compared to normotensive patients. The study also showed that hypertensive patients with target-organ damage have the lowest scores in emotional and physical aspects, vitality, and mental health component summary scores.[57] The possible causes include adverse effects from medication, diseases associated with HT and simply being diagnosed with the disease, since it is related to increased mortality. All these factors can decrease a patient's QOL.

Systolic HT is common in type 2 DM, and may affect the majority of diabetic patients at some point in the disease process. HT is an important modifiable risk factor in the micro and macrovascular disease.

In this study, patients were already diagnosed with HT according to the South African Hypertension Guidelines. The diagnosis was not further delved into.

- Dyslipidaemia: Atherosclerosis accounts for up to 70% of all diabetic mortality in white, coloured and Asian patients. Atherosclerosis is still uncommon in the black population as compared to Caucasian and Indian patients, but is on the rise. Lipid abnormalities are common in diabetic patients and are an important contributor to the high incidence of vascular disease. The most frequently encountered lipid abnormalities in diabetic patients are increased serum triglyceride levels and decreased serum HDL cholesterol levels.[32]

HT and dyslipidaemia were included as separate variables. This was done so that the number of co-morbidities a patient suffered from could be documented, as well as the added pill burden.

Psychosocial factors such as health-related beliefs, social support, coping mechanisms, and personality type may have a compelling effect on QOL. These effects may be direct, or indirect, buffering the negative impact of diabetes or its demands. In fact, these psychosocial factors may be the most powerful predictors of QOL, often outweighing the effects of important disease-related factors, such as glucose control and complications.[12]

Chapter 2: MOTIVATION FOR STUDY

Successful management of diabetes can be challenging especially if patients are non-compliant to treatment. This is because the management and abating of complications is largely patient driven. It is important to remember that the disease not only affects the individual, but affects the patient's family, friends and the community. Successful management of DM requires a holistic approach with attention to the behavioural, psychological and social aspects of this chronic, progressive condition.

Patient's attitude towards their disease and treatment ultimately dictates how much of the doctor's advice will be used or discarded; and how compliant patients will be to their treatment regimen. It is important to note that complications of DM have a significant impact on the patient's QOL, morbidity and mortality. Greater insight into HRQOL is the key to the successful management of DM.

Furthermore, there is a lack of South Africa specific information. While there may be no reason to suggest that SA is different to other countries and the results obtained, country specific information may provide a greater insight into the treatment and impact of middle-income and developing countries, whose future relies on the health of the population. The contribution to clinicians and researchers will also be useful regarding clinic audits and providing insight into patient habits.

The purpose of this study was to have a better understanding of the effects of diabetes on HRQOL, and which diabetic parameters determine this. The findings of this research will hopefully contribute to a better understanding and a more effective treatment regimen with improved compliance to treatment and a decrease in diabetic complication rates.

Chapter 3: STUDY DETAILS

3.1 Aims and Objectives

a) To determine the HRQOL of a sample of type 2 diabetic patients.

b) To describe the demographics (age, gender, smoking pack year history, number of alcohol units consumed per week etc.) of the population being studied.

c) To document the following parameters which are important in determining the control and severity of type 2 diabetes:

   I. Glycosylated haemoglobin (HbA_{1C})
   II. Determine the patient's total amount of insulin required per day (if on insulin therapy).
   III. Body Mass Index (BMI)
   IV. Exercise compliance

d) To determine whether there is an association between any or all of the above parameters and the HRQOL of these patients.

e) To determine the presence of any co-existing diseases and compare HRQOL between diabetic patients with and without co-existing diseases:

   I. Hypertension (HT)
   II. Dyslipidaemia

3.2 Study Design

This was a clinical audit, cross-sectional in nature, and descriptive study of consecutive patients attending the diabetic clinic from June to September 2012.

3.3 Study Setting

The study was conducted at the Diabetic Clinic, in Helen Joseph Hospital (HJH), Johannesburg, Gauteng. This institute is a Level 3 state hospital that provides healthcare services to patients across the Gauteng province. The clinic caters for only diabetic patients, type 1 and 2, however type 2 patients predominate. A team consisting of clinicians, physiotherapists, diabetic educators and dieticians manage the care of patients.

3.4 Study population

The study population consisted of 200 patients attending the diabetic clinic at the Helen Joseph Clinic (HJH). This sample size was chosen to include all patients who met inclusion criteria and get a fair representation of the population attending the diabetic clinic. HJH is a state owned hospital, and the study assumes that the individuals attending this clinic are individuals from a lower socio-economic status, that do not have access to private healthcare.

3.5 Inclusion Criteria

i. Patients attending the specialist Diabetic Clinic
ii. Patients with type 2 DM
iii. Patients attending Diabetic Clinic for 6 months or longer

3.6 Exclusion Criteria

i. Patients with type 1 DM
ii. Patients who are blind (as they could not fill in the questionnaire)
iii. Patients from whom informed consent could not been obtained

3.7 Methodology

Consecutive diabetic patients were handed the questionnaire forms when they attended the clinic for their routine consultation. Patients were informed that this is a confidential study and ethical approval had been granted by University of the Witwatersrand Human Research Ethics Committee. The purpose of the study was explained and they had the option to refuse to participate if they so desired. No incentives were offered for participation nor were they discriminated against if they refused to participate (Appendix 1). Patient consent forms were in English only. While English may not have been the first language for the patients, nurses at the HJH hospital assisted patients to facilitate the completion of the questionnaire. According to Zikmund (2003)[119], when individuals are assisted to complete the questionnaire, they may provide socially acceptable answers, and not truthful answers. This is acknowledged and was taken into account when data was analysed.

Once informed consent was obtained from patients who fulfilled the inclusion criteria, patients were asked to complete the D-39 questionnaire (Appendix 2) combined with a questionnaire gathering demographic data (Appendix 3). Patients completed the questionnaire while awaiting their consultation or after being seen by the doctor. Patients were not allowed to take the questionnaire home. There was no time limit on the duration of answering the questionnaire. Patients then inserted the questionnaire into a sealed box, regardless of it being completed or not.

In order to maintain patient confidentiality, a number corresponding to the numbered questionnaire form was attached to the patient's file (Appendix 4). The patient's name was not recorded on the questionnaire. Each patient was allocated a unique patient identification number in the sequence that they entered the study. Only the principal investigator had access to the list linking patients' names and unique identification numbers.

The questionnaire captured demographic variables such as age, gender, age of diagnosis, marital status, exercise regimen, employment status, living arrangements, smoking and alcohol habits, height, weight, as well as diabetes-specific variables such as concurrent use of antihypertensive medication and/or lipid lowering drugs.

The patient's files were then analysed and various diabetic parameters (HBA_{1C}, lipogram, weight, height, number of insulin units used per day and the whether there was any concurrent use of OHA) were noted. (Appendix 5)

3.8 Definitions

Health Related Quality of Life: (HRQOL)

The Diabetes-39 (D-39) questionnaire was used to determine the quality of life (QOL) of the patients. QOL was not defined to respondents during the development of the D-39 questionnaire.[21]

No attempt was made to define QOL to the patients during this study; instead patients were asked to grade and indicate the effect of each item on their QOL according to their own interpretation. The grading scale ranged from 1 (not affected) to 7 (severely affected).

Diabetes

The study was confined to patients with type 2 DM, all of which were previously diagnosed according to the ADA guidelines. Unless otherwise proven, it was assumed that patients had type 2 DM if they were diagnosed after the age of 30 years. Patients under the age of 18 years for ethical reasons and patients with type 1 DM were excluded.

Exercise

Patients were deemed to be exercising if they attended a gymnasium/ sporting/ recreational facility at least 3 times per week or if they reported doing an exercise routine routine by themselves for at least 30 minutes, three times per week. This routine must have been followed for at least 1 month.

Patients were asked to describe the type of exercise they did if they self-exercised. This was done to ensure that activities such as “window shopping” or domestic work were not considered exercise. The type of exercise i.e. whether they exercised in a gymnasium/sporting or recreational facility or self -exercised, was not pursued further in this study.

Dyslipidaemia

Dyslipidaemia was considered to be present if patients were on any type of lipid-lowering therapy or had a total cholesterol >5.0, HDL <1.2 in females or < 1.0 in males, triglyceride > 1.7 or a LDL >3.0 mmol/L. The study did not differentiate between the types of lipid-lowering therapies used.

Hypertension

Patients were defined as having HT if either the systolic blood pressure was > 140 mmHg and/or the diastolic blood pressure was >90 mmHg or if they were on any concurrent antihypertensive treatment. The study did not distinguish between the types of antihypertensive agents.

3.9 Statistical analysis

Data was collected initially on individual questionnaires, and then transcribed into data collection sheets in Microsoft Office ® Excel 2007 spread sheet. Data analysis and coding was computed using Microsoft Excel 2007, and IBM SPSS version 20.

Data was checked for normality (normal distribution); however as is common with social studies, normality is not always achieved. In order to mitigate against this, data was

bootstrapped 100,000 times to ensure that sufficient variance existed in the data and the results obtained can be confidently interpreted.

Descriptive statistics including means, medians, modes, standard deviations and inter-quartile ranges were performed where appropriate. In addition to the descriptive statistics, a principle component analysis (PCA) was performed. PCA allowed for the reduction in the number of variables for analysis and subsequently allowed for the variables explaining the largest amount of variance to be analysed in the context of the objectives of the study.

In order to understand if there are factors influencing the QOL, associations between variables were analysed, using the Spearman's correlation co-efficient. It is important to note that the associations are not to be interpreted to be causal factors.

Continuous data are presented as median values with interquartile ranges and categorical data are described using proportions. Student t-tests for unpaired data were performed to compare medians between groups when the data were normally distributed; Mann-Whitney tests were used when the data were not normally distributed. Fisher's exact test was used to compare categorical variables between groups. P value ≤ 0.05 was considered significant.

3.10 Measurement Instrument

3.10.1 Health Related Quality of Life Instrument:

Written permission was obtained to use the D-39 questionnaire from the authors (Appendix 6). The instrument encompasses measurements of energy and mobility (EM); diabetes control (DC); anxiety and worry (AW); social burden (SB); and sexual functioning (SF).

Respondents were asked “how much was the quality of your life affected by” a wide range of aspects of diabetes illness and its treatment in the past month. Items are administered using seven response categories, ranging from not affected at all (score = 1) to extremely affected (Score = 7). A sample of the questionnaire can be found in Appendix 2.

The scoring instructions obtained from the developers, dictated the following:
If more than 4 items were missing (excluding missing items in Sexual Functioning, some respondents either refused or were unable to answer these questions considering the special treatment of this sensitive scale) the questionnaire was excluded from the analysis.

No value was presented for scales, when a certain number of items were missing and the scale was then not scored:

Diabetes Control – 3 items

Anxiety and Worry – 1 item

Social Burden – 1 item

Sexual Function – 0 items

Energy and Mobility – 3 items

With the above borne in mind, the subscale scores were calculated by summing responses across all items in the same subscale, with high scores representing poor HRQOL. To facilitate comparison of scale scores in the validity and reliability research, each of the 6 scale scores were transformed to 0 – 100 scale. A single algorithm for making this transformation was followed.

The algorithm:

$$TSS = [(RSS – LPSS) / PSSR] \times 100\%$$

Where: TSS = Transformed Scale Score; RSS = Raw Scale Score; LPSS = Lowest Possible Scale Score; HPSS = Highest Possible Scale Score; PSSR = Possible Scale Score Range;

Therefore for each component the score was derived from these formulae:

Diabetes Control: [(Raw scale score – 6) / (90 – 6)] x 100

Anxiety and Worry: [(Raw scale score – 2) / (30-2)] x 100

Social Burden: [(Raw scale score – 2.5) / (37.5 – 2.5)] x 100

Sexual Functioning: [(Raw scale score – 1.5) / (22.5 – 1.5)] x 100

Energy and Mobility: [(Raw scale score – 7.5) / (112.5 – 7.5)] x 100

The reliability of the D-39 questionnaire is acceptable with a Cronbach alpha of 0.81-0.93 for all the sub-scales. The construct validity was compared with the widely used SF-36 and found to be very satisfactory.[15] The researchers that developed the D-39 questionnaire did not give express consideration to face/content validity but used extensive literature reviews,

existing QOL questionnaires and interviews with health professionals and diabetic patients to develop the questionnaire.[11]

The D-39 diabetes-specific QOL measure has been recommended for use in research and clinical settings.[23,98,99] The instrument provides evidence for validity and reliability, includes several domains that cover various aspects of QOL, and therefore is applicable to a wide population of patients.[19,23,98,99] The D-39 is one of few diabetes-specific QOL measures that have been shown to be responsive to changes in health status.[93] Importantly, this instrument does not impose a definition of QOL upon patients, but instead allows patients to respond in the context of their personal conceptualization of QOL.[19] These attributes make the instrument highly patient-centered, one of the most critical components to any patient-assessed QOL measure.[42]

The questionnaire and scoring instructions obtained from the developers of the questionnaire are as follows:

3.10.2 Diabetes Control

Twelve of the thirty-nine questions measure the effects of 'diabetes control' on the patient's QOL. Table 1 below provides the corresponding questions that measured diabetes control on the D-39 questionnaire, by asking patients to respond to how much the quality of an individual's life has been affected by:

Table 1: Corresponding question from D-39 questionnaire measuring the impact of Diabetes Control on QOL

Question number on D-39 Questionnaire	**Question**
Question 1	Your daily medication for your diabetes
Question 4	Following your doctor's prescribed treatment plan for diabetes
Question 5	Food restrictions required to control your diabetes
Question 14	Having diabetes
Question 15	Losing control of your blood sugar levels
Question 17	Testing your blood sugar levels
Question 18	The time required to control your diabetes
Question 24	Getting your diabetes well controlled
Question 27	Keeping a record of your blood sugar levels
Question 28	The need to eat at regular intervals
Question 31	Diabetes in general
Question 39	Having to organize your daily life around diabetes

This score determines the effect of all the measures that the patient takes to maintain normal blood glucose levels. As instructed by the developers of the questionnaire, at least 9 out of the 12 questions need to be answered for the result to be meaningful. The higher the score

that was achieved, the poorer was the QOL i.e. 6 is the best possible QOL and 90 represents the worst possible QOL.

3.10.3 Anxiety and Worry

Four questions of the thirty-nine questions are related to this aspect of QOL.
Table 2 below provides the corresponding questions that measured anxiety and worry on the D-39 questionnaire, by asking patients to respond to: During the past month how much was the quality of life affected by:

Table 2: Corresponding question from D-39 questionnaire measuring the impact of Anxiety and Worry on QOL

Question number on D-39 Questionnaire	**Question**
Question 2	worries about money matters
Question 6	concerns about your future
Question 8	stress or pressure in your life
Question 22	feeling depressed or low

These quantify the anxiety and worry that having diabetes is causing in the patient's life. The authors of the questionnaire suggest that a minimum of 3 out of the 4 questions needs to be answered for the result to be meaningful. The higher the score that was achieved, the worse was the QOL.

3.10.4 Social Burden

Five of the thirty-nine questions relate to this aspect of patient's QOL.

Table 3 below provides the corresponding questions that measured social burden on the D-39 questionnaire, by asking patients to respond to: During the past month how much was the quality of life affected by:

Table 3: Corresponding question from D-39 questionnaire measuring the impact of Social Burden on QOL

Question number on D-39 Questionnaire	**Question**
Question 19	The restrictions your diabetes places on your family and friends
Question 20	Being embarrassed because you have diabetes
Question 26	Doing things that your family and friends don't do
Question 37	Being identified as a diabetic
Question 38	Having diabetes interfere with your family life

It is a measure of the burden that diabetes is having on the patient's social life. Authors of the questionnaire suggest that a minimum of 4 questions need to be answered for the result to be meaningful. A higher social burden indicates a lower QOL.

3.10.5 Sexual Functioning

Three of the thirty-nine questions are related to how much their sexual functioning has affected their QOL.

Table 4 below provides the corresponding questions that measured sexual function on the D-39 questionnaire, by asking patients to respond to: During the past month how much was the quality of life affected by:

Table 4: Corresponding question from D-39 questionnaire measuring the impact of Sexual Functioning on QOL

Question number on D-39 Questionnaire	Question
Question 21	Diabetes interfering with your sex life
Question 23	Problems with sexual functioning
Question 30	A decreased interest in sex

The authors of the questionnaire maintain that all 3 questions need to be answered for the result to be meaningful. Due to the sensitivity of these questions, some participants either refused to answer or ignored these questions. In the event of this occurring, the questionnaire and the participant were excluded from the study. The higher the score that was achieved, the worse was the QOL.

3.10.6 Energy and Mobility

Fifteen of the thirty-nine questions in the Diabetes-39 questionnaire quantify how much diabetes is affecting the patient's energy and mobility levels. Table 5 below provides the corresponding questions that measured energy and mobility on the D-39 questionnaire, by

asking patients to respond to: During the past month how much was the quality of life affected by:

Table 5: Corresponding question from D-39 questionnaire measuring the impact of Energy and Mobility on QOL

Question number on D-39 Questionnaire	**Question**
Question 3	Limited energy levels
Question 7	Other health problems besides diabetes
Question 9	Feelings of weakness
Question 10	Restrictions on how far you can walk
Question 11	Any daily exercises for your diabetes
Question 12	Loss or blurring of vision
Question 13	Not being able to do what you want
Question 16	Other illnesses besides diabetes
Question 25	Complications from your diabetes
Question 29	Not being able to do housework or other jobs around the house
Question 32	Needing to rest often
Question 33	Problems in climbing stairs or walking up steps
Question 34	Having trouble caring for yourself (dressing, bathing, or using the toilet
Question 35	Restless sleep
Question 36	Walking more slowly than others

The authors of the questionnaire suggest that 12 of the questions need to be answered for the result to be meaningful. If 4 or more of the questions were unanswered, the questionnaire was excluded from the study. The higher the score that was achieved, the poorer was the QOL.

3.11 Severity and control of diabetes

The following measurements of the severity and control of diabetes were obtained from patient files (Appendix 3, 4):

- Demographics (age, gender)
- Smoking pack year history (number of cigarettes smoked per day divided by pack of 20 cigarettes multiplied by number of years smoked). This study did not measure factors such as brand and strength (nicotine and tar content).
- Alcohol units consumed per week. This study did not distinguish between types of alcohol consumed (wine, spirits etc.)
- Number of insulin units used per day. This study did not distinguish between the types of insulin used (i.e. rapid or long acting insulin) or the amount of times a patient injected him/herself (daily or twice daily regimens)
- Use of antihypertensive, lipid lowering medication or OHA
- Exercise (see definition on page 18-19). This study did not distinguish between the grades of physical activity.
- Weight was measured using a standard calibrated scale placed on the floor. Patients were weighed while standing barefoot and were instructed not to hold onto any form of support.

- Height was measured with a tape measure and recorded to the nearest centimetre. The patient was requested to stand barefoot with his/her heels together and touching the wall, with his/her back against a wall.
- BMI. This was calculated using the Quetelet's formula- weight (kg)/height^2 and was defined using WHO classification.
- Most recent Lipid profile and
- Latest HBA_{1C} level

Chapter 4: RESULTS

Data from 200 patients were analysed in the study from the Diabetic Clinic at Helen Joseph Hospital. While data was collected from 220 patients, 20 patients were excluded from the study due to incomplete questionnaire (14 patients) or lack of data recorded in the file (6 patients). 10 patients refused to participate in the study.

4.1 Demographics

4.1.1 Age and gender

Table 1, shows the demographic profile of the patients analysed; A higher proportion of females participated in the study (57% vs. 43%). The mean age of the study group was 55.89 years (SD±12.52 years), with the youngest subject aged 30 years and the oldest subject aged 82 years. Median age was 58 years. Mean age of males was 53.29 (SD±12.73) and females was 57.8 years (SD±12.04)

Table 6: Demographic profile of the study sample. Data are expressed as number (interquartile range)

Parameter	**Results**
Total no. of patients	200
Gender:	
Males	86 (43%)
Females	114 (57%)
Age (years):	
Median	40
Range	30 – 82
Male Median ±SD	56 ± 12.73
Female Median ±SD	60 ± 12.04

Table 6 indicates the age profile of individuals, and allows one to understand the age and gender of individual's that are presently being treated with type 2 DM.

4.1.2 Age of diagnosis of diabetes

In the sample group of 200, the earliest age of being diagnosed with DM was age 18 and the oldest being age 72. The mean age of diagnosis was 42.19 years (SD ± 10.74). Due to the age range, the median age was used in the analysis to mitigate against the influence of outliers in the subsequent statistics on age.

Table 7: Age of diagnosis of the study sample. Data are expressed as number (interquartile range)

Parameter	Results
Median	40
Range	18 - 72
Male Mean ±SD	41.34 ± 10.81
Female Mean ±SD	42.82 ± 10.69

4.1.3 Employment status

Of the 200 patients, 24.5 % (49 patients) were employed whilst the remaining 75.5 % (151 patients) were unemployed.

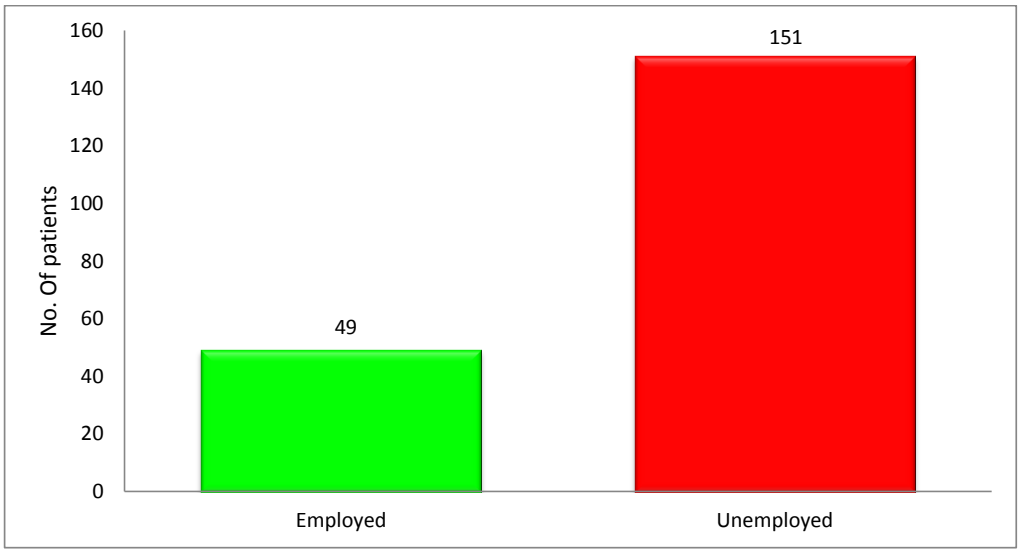


Figure 1: Employment status of patients presenting with Diabetes at HJH

4.1.4 Living arrangements

Of the 200 patients, 13 % (26 patients) lived alone while 87 % (174 patients) lived with family members.

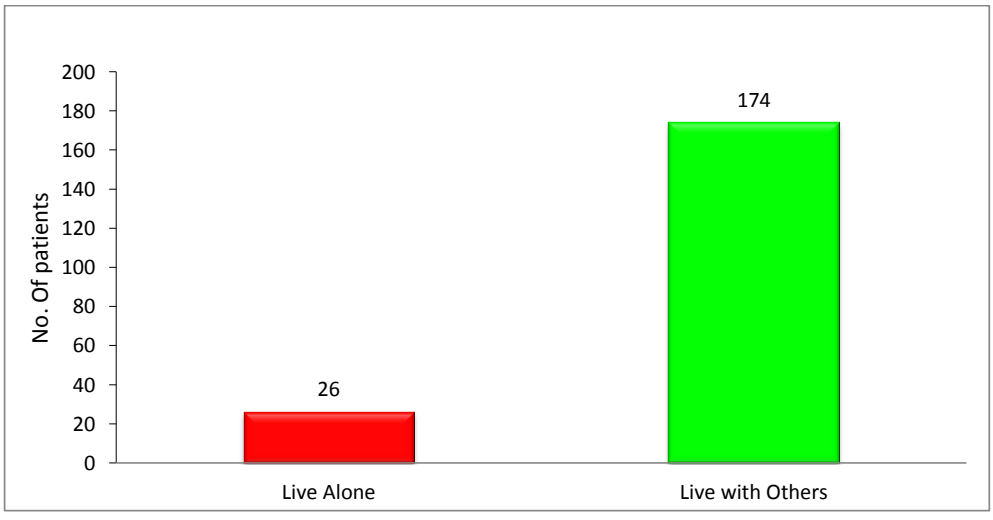


Figure 2: Living arrangements of patients presenting with Diabetes at HJH

4.2 Recreational Habits - Cigarette and alcohol use

4.2.1 Cigarette smoking:

Sixty-nine and a half percent of the patients analysed did not smoke. Smoking pack year history (number of cigarettes smoked per day divided by number of cigarettes in a cigarette pack multiplied by number of years smoked) ranged from 0.1 to 60 for those who smoked. For descriptive purposes, patients who smoked cigarettes were grouped into 4 categories based on their smoking pack year history:

- 0.1 – 10 pack year history
- 10.1 – 20 pack year history
- 20.1 – 40 pack year history
- ≥ 40.1 pack year history

Table 8: Smoking pack year history of the sample

Smoking Pack Year History	No. of Patients
0	139 (69.5%)
0.1 - 10	32 (16%)
10.1 - 20	17 (8.5%)
20.1 - 40	9 (4.5%)
40.1+	3 (1.5%)

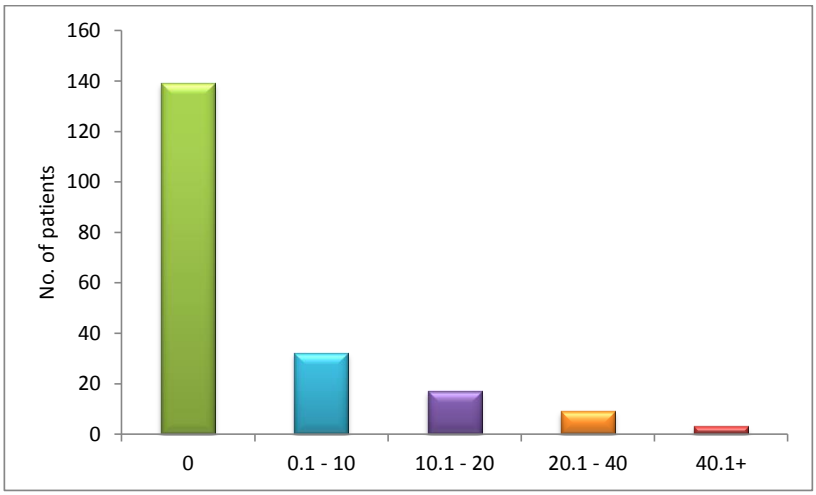


Figure 3: Graphic representation of no of pack years per smoking (x-axis) and number of patients smoking (y axis)

4.2.2 Alcohol consumption

Eighty-four and a half percent (169 patients) of the sample population did not consume alcohol; while fifteen and a half percent (31 patients) of the sample consumed some alcohol. The study did not distinguish between the type of alcohol consumed (i.e. wine, spirits, brandy, whiskey etc.). The mean consumption of the sample was 0.525 units per week (SD 1.537). The range of consumption in the sample was 0 to 10 units per week. For description purposes, weekly alcohol consumption was grouped into 2 categories:

- 0.1 – 5 units per week
- 5.1-10 units per week

Table 9: Alcohol consumption per week of the sample

Alcohol units consumed per week	No. of People
0	169 (84.5%)
0.1 - 5	28 (14%)
5.1 - 10	3 (1.5%)

4.3 Concurrent anti hyperglycaemic agent use:

4.3.1 Metformin

Of the 200 patients, 65% (130 patients) were using metformin concurrently with their insulin regimen, while 35% (70 patients) used insulin alone.

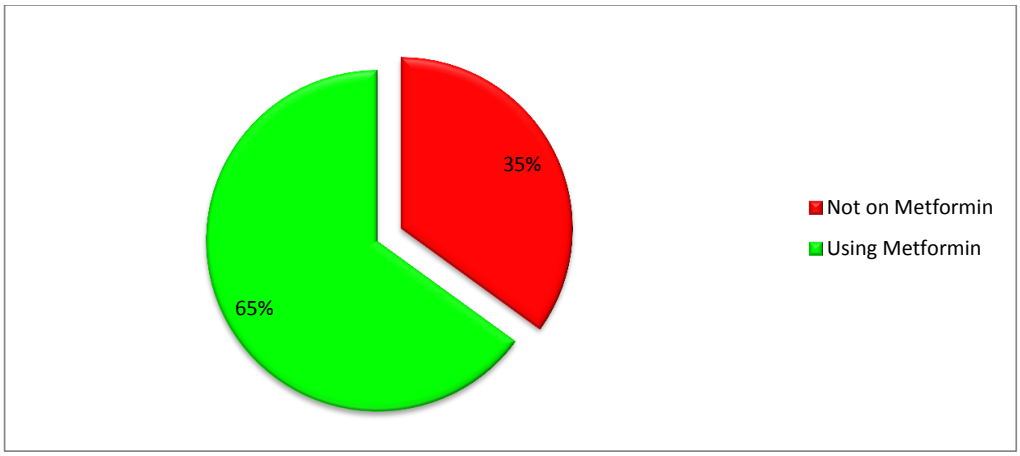


Figure 4: Metformin use in the sample

4.3.2 Sulphonylurea

Eighty-eight percent (176 patients) of the 200 patients used sulphonylurea concomitantly, while twelve percent (24 patients) were not using sulphonylurea.

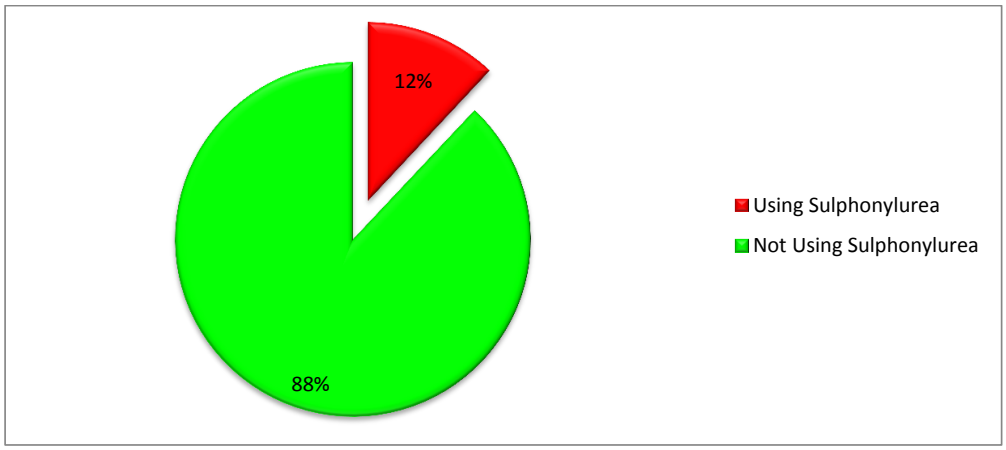


Figure 5: Sulphonylurea use in the sample

4.3 Exercise

Fifty-three percent (106 patients) of the total group exercised regularly, while forty-seven percent (94 patients) did not exercise.

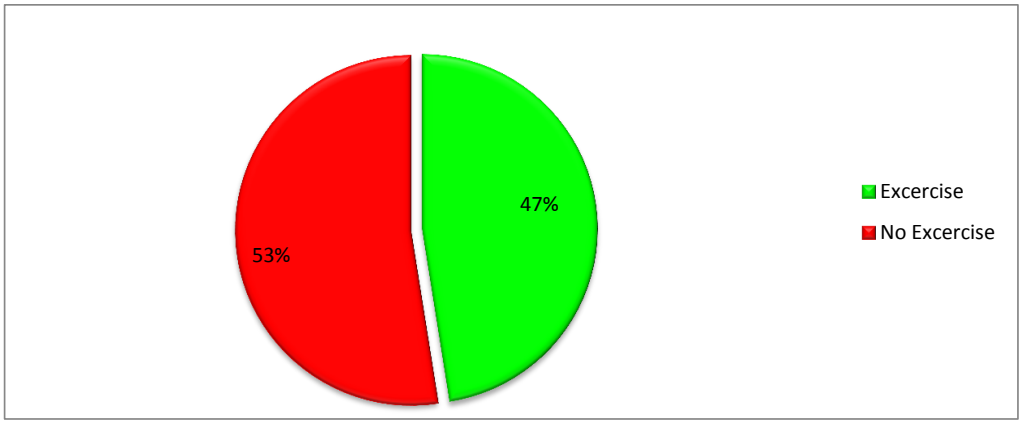


Figure 6: Exercise in the sample

4.4 Insulin usage

Of the sample of 200 patients, 99.5 % (199 patients) used insulin, whilst 0.5 % (1 patient) used oral hypoglycaemic agents only. For descriptive purposes the total number of insulin units used per day, were divided into 7 categories and it shown in table 10 below:

Table 10: Insulin units used per day

No. of insulin units/per day	No. of People
0	1
0.1 - 40	63
40.1 -80	89
80.1 - 120	25
120.1 - 160	3
160.1 -220	4

4.5 Co-existing diseases:

4.5.1 Hypertension (HT)

The sample is skewed to people with high blood pressure, due to the data collected at a diabetic clinic. The significant difference ($p<0.05$) between the number of individuals with HT and dyslipidaemia and people with no HT and dyslipidaemia, therefore limiting the interpretation of the results.

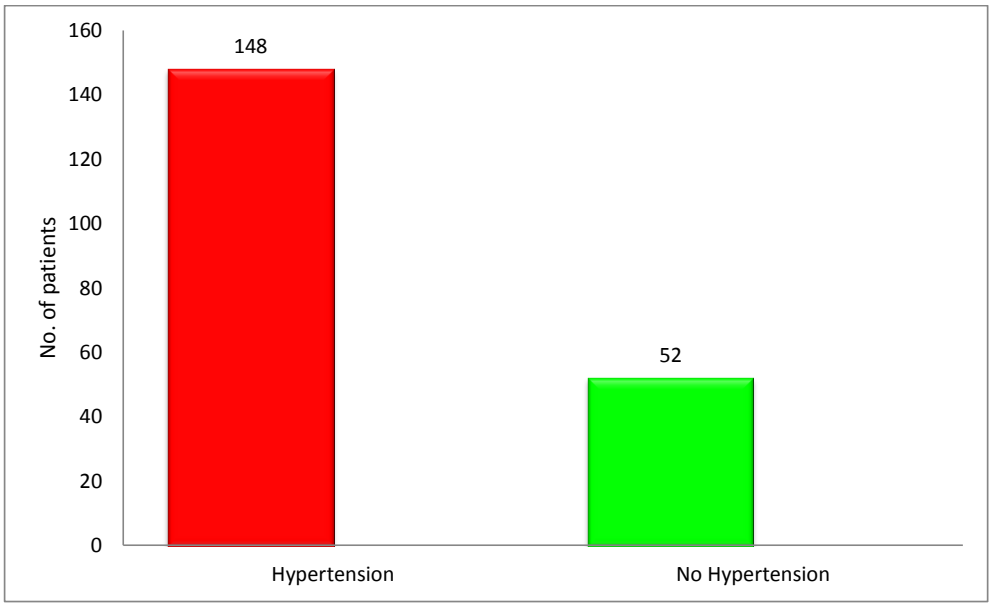


Figure 7: Hypertension in the sample

Of the 200 patients, 74 % (148 patients) in the sample had HT as well as type 2 DM as opposed to having type 2 DM alone. The remaining 26 % (52 patients) had normal blood pressure. The study did not delve further into the type/class of antihypertensive agents the patients used.

4.5.2 Dyslipidaemia

Of the 200 patients, 70 % (140 patients) of the sample population used lipid lowering medication in conjunction with their diabetic medication. 30 % (60 patients) however, did not have dyslipidaemia. All the patients were on statins.

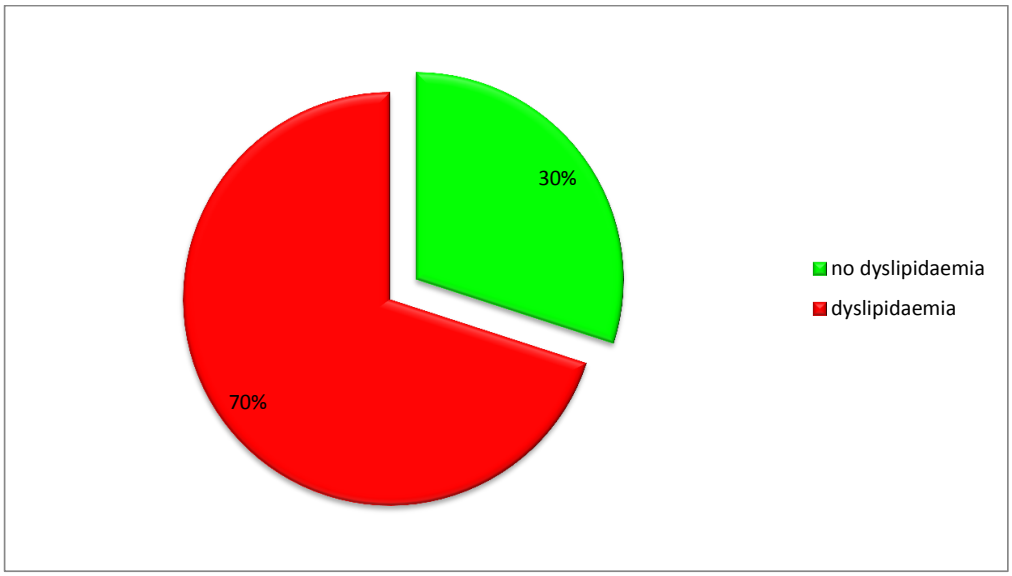


Figure 8: Dyslipidaemia in the sample group

4.6 HBA$_{1C}$

For descriptive purposes, patients were grouped into 5 categories:

- HbA$_{1C}$ less than 7%
- HbA$_{1C}$ between 7 – 7.9%
- HbA$_{1C}$ between 8 – 8.9%
- HbA$_{1C}$ between 9 – 9.9%
- HbA$_{1C}$ greater than 10%

Of the 200 patients, 14% (28 patients) had the target HbA$_{1C}$ of less than 7%. 14% (28 patients) had an HbA$_{1C}$ of between 7% and 7.9%. 11.5% (23 patients) had an HbA$_{1C}$ of between 8% and 8.9%. 20.5% (41 patients) had an HbA$_{1C}$ between 9% and 9.9% and 40% (80 patients) had an HbA$_{1C}$ greater than 10%.

The mean HbA$_{1C}$ in this study was 9.5%. The mode was 9.7% with 9 patients having this level. (Range 4.5 % – 17.6%). The standard deviation of HbA$_{1C}$ of the sample was 2.4% .

Table 11: HBA_{1C} of the sample

HBA_{1C}	No. of People
≤ 7%	28 (14.0 %)
7.1 - 7.9 %	28 (14.0 %)
8 - 8.9 %	23 (11.5 %)
9 - 9.9 %	41 (20.5 %)
≥ 10 %	80 (40.0 %)

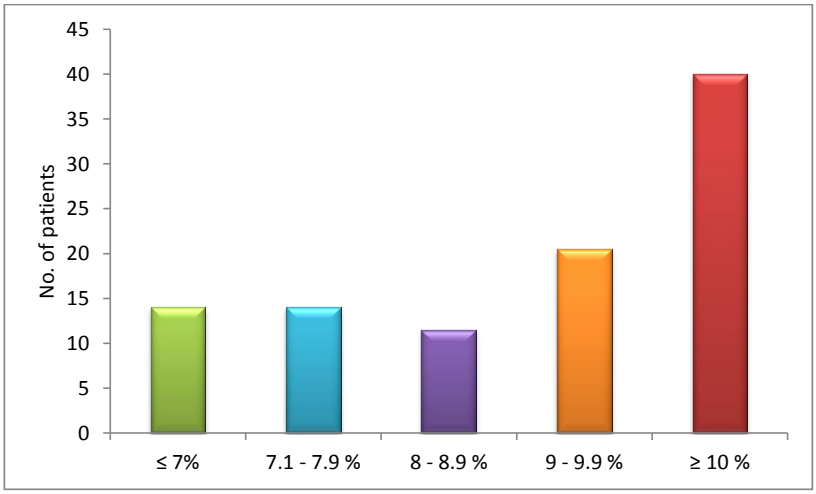


Figure 9: HBA_{1C} analysis

4.7 Lipogram

Each lipogram has 4 components; total cholesterol measured in mmol/l, triglyceride level in mmol/l, HDL in mmol/l and LDL in mmol/l. For descriptive purposes each value has been shown separately in the tables below.

4.7.1 Total cholesterol (TC)

According to the 2012 SEMDSA guidelines, ideal total cholesterol level is ≤ 4.5 mmol/l. For descriptive purposes the total cholesterol was divided into 5 categories. As shown below, 57% (114 patients) of the 200 sample reached target cholesterol levels.

Table 12: Total cholesterol levels of the sample

Total cholesterol in mmol/l	No. of People
≤ 4.5	114
4.6 - 4.9	23
5.0 - 6.0	43
6.1 - 7.0	16
≥ 7.1	9

4.7.2 Triglyceride (TG)

According to the 2012 SEMDSA guidelines, ideal triglyceride level is ≤ 1.7 mmol/l. for the purposes of the study, the triglyceride levels were divided into 5 categories. 61.5% (123 patients) reached target levels.

Table 13: Triglyceride levels of the sample

Triglyceride level in mmol/l	No. of People
≤ 1.7	123
1.8 - 2.5	39
2.6 - 3.5	24
3.6 - 4.5	12
≥ 4.6	7

4.7.3 High Density Lipoprotein (HDL)

According to the 2012 SEMDSA guidelines, target HDL levels for female patients are 1.2 mmol/l, whilst for men is 1.0 mmol/l. For descriptive purposes the HDL levels were divided into 5 categories. 64.5% (129 patients) reached target.

Table 14: HDL levels of the sample

HDL mmol/l	No. of People
≤ 1.2	129
1.3 - 2.0	61
2.1 - 3.0	9
3.1 - 4.0	2
≥ 4.1	4

4.7.4 Low density lipoprotein (LDL)

LDL is preferred when deciding on treatment and assessing its effect. LDL cholesterol is used in preference to other lipid tests as it is modifiable by treatment and the beneficial effects of lowering LDL levels are well known. LDL can be measured directly or can be calculated from the Friedewald equation (in mmol/l), where LDL = TC – HDL – TG/2.2, provided the TG level does not exceed 4.5 mmol/l. In this study LDL levels were calculated using the Friedewald formula and were not reported if the triglyceride level was > 4.5 mmol/L.

According to the 2012 SEMDSA guidelines, target LDL levels in diabetic patients are 1.8 mmol/l. For descriptive purposes the LDL levels were divided into 5 categories. 24.5% (49 patients) of the sample size reached target. 1 patient had a too high triglyceride level thus the LDL level could not be calculated by the NHLS.

Table 15: LDL levels of the sample

LDL mmol/l	No. of People
≤ 1.8	49
1.9 - 2.5	66
2.6 - 3.5	55
3.6 - 4.5	20
≥ 4.6	10
blank	1

4.8 Body Mass Index (BMI)

This is the weight in kilograms divided by the height in meters squared expressed as kg/m^2.

Patients were classified as:

- underweight (BMI <20kg/m^2),
- normal (BMI 20 to 24.9kg/m^2),
- overweight (BMI >25 to 29.9kg/m^2),
- Obese (BMI >30kg/m^2).

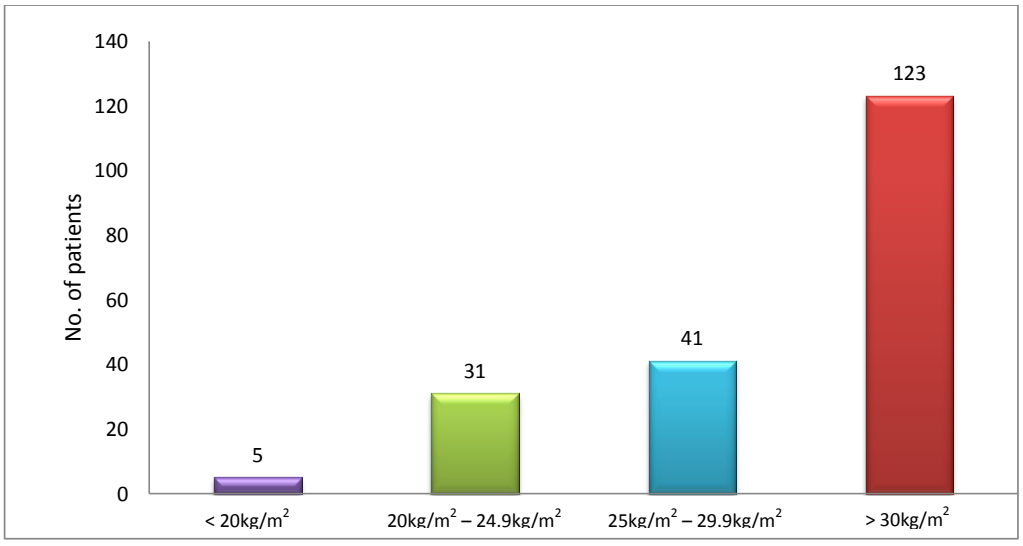


Figure 10: BMI categories of the sample group

2.5% (5 patients) were in the underweight category. Only 15.5% (31 patients) were in the normal weight category. 20.5% (41 patients) were in the overweight category and 61.5% (123 patients) were in the obese category i.e. 82.0% of patients were above ideal BMI in this study. Of the 123 patients in the obese category, 60% (74 patients) were female and 40% (49 patients) were male.

4.9 Health Related Quality of Life (HRQOL) scores

The 5 aspects of QOL of the D–39 questionnaire (Energy and Mobility; Sexual Functioning; Social Burden; Anxiety and Worry; and Diabetes Control) and while all these factors influence impact the HRQOL and are as follows:

Overall Ratings

Table 16: Linear transformed ratings

	Diabetic Control	Anxiety & Worry	Social Burden	Sexual Function	Energy & Mobility
Mean Total	43.65	53.77	32.76	51.76	38.91
Mean Male	39.63	51.58	30.66	59.86	35.2
Mean Female	46.66	55.42	34.34	45.66	41.71

4.9.1 Diabetes Control

Khanna et al., 2012 and MK Tulloch-Reid; SP Walker (2009) report that on a transformed scale of 0-100, a score closer to 0 indicates a better QOL, while a score closer to 100, a

worse QOL. The results indicate that the mean sample score for diabetic control of 43.65, indicating that when diabetes is controlled, individuals have a better perceived QOL.

4.9.2 Anxiety and Worry

Scores closer to 0 indicate a better quality of life. The higher the score that was achieved the worse was the QOL. The total mean score was 53.77. The male mean was 51.58 and the female mean was 55.42. 19 patients had a score of 71.43 (mode). (Range 7.14 – 235.71).

4.9.3 Social Burden Score

The possible scores ranged from 7.14 to 92.86. The higher the score achieved the worse was the QOL. The total mean score of the patients was 32.76. The male mean was 30.66 and female mean was 34.34. The mode was 7.14 with 22 patients achieving this score.

4.9.4 Sexual Functioning Score

The higher the score that was achieved the worse was the QOL. The total mean score was 51.76. Female mean score 45.66 and for males was 59.86. The score most commonly recorded (mode) was 7.14 with 35 patients achieving this score. (Range 2.38 – 92.86).

4.9.5 Energy and Mobility Score

The total mean score for this sample of patients was 43.65. The higher the score achieved the worse was the QOL. The female mean score was 46.66 and the male mean was 39.63. The most frequently observed score (mode) was 36.90 which was scored by 12 patients. (Range 7.14 – 92.86)

While the above indicates the HRQOL factors, further analysis on the factors which individuals perceive to influence QOL were subjected to a principle components analysis. **The results indicate that sexual function, anxiety and worry and diabetes control are the factors that mainly influenced the HRQOL in this study.**

Principle Components Analysis 1(PCA) was most influenced by sexual function alone explaining 71% of the variation observed, while PCA 2 is influenced by anxiety and worry (47%) and diabetes control (38%).

Table 17: Principle Component Analysis (PCA)

	PCA 1	PCA 2
Sexual Function	0.71	-0.69
Anxiety & Worry	0.53	0.47
Social Burden	0.30	0.29
Diabetes Control	0.27	0.38
Energy & Mobility	0.19	0.24

Table 17 above indicates that the sexual function accounts for the most variation in the dataset from all the constructs that measure QOL. This may indicate that QOL is perceived as the most important factor amongst patients with diabetes and measurement of QOL.

4.10 Association between parameters influencing QOL

In order to understand if an association between the parameters measured and HRQOL, Pearson's correlation co-efficient was computed.

A complete table of the results is presented in Appendix 7.

Table 18: Significant associations (p<0.05 and p<0.01) between HRQOL and parameters

	HRQOL	High BP	High Chol	Diabetes Control	Anxiety/Worry	Social Burden	Sexual Function	Energy/ Mobility	HBA_{1C}
HRQOL	1								
High BP	-.232**	1							
High Cholestrol	-.301**	.607**	1						
Diabetes Control	.745**	-.174*	-.306**	1					
Anxiety/ Worry	.781**	-.064	-.171*	.603**	1				
Social Burden	.728**	-.076	-.191**	.573**	.469**	1			
Sexual Function	.667**	-.187**	-.167*	.186**	.344**	.270**	1		
Energy Mobility	.606**	-.362**	-.294**	.532**	.296**	.464**	.167*	1	
HBA_{1C}	-.155*	.069	.041	-.166*	-.045	-.214**	-.082	-.086	1

Table 18 below indicates that significant associations (p<0.05).

Key to above table: Red shaded cells: Significant at the 0.01 level

Yellow shaded cells: Significant at the 0.05 level

Clear cells: Not significant at any p-value

Chapter 5: Discussion

5.1 Demographics

A mean age of 55 years for diabetics in this study is consistent with the WHO declaration that type 2 DM is more common in the older generation in developing countries. There were more females (57%) than males (43%) in this study. Of the 200 patients, 79 were above the age of 60 years.

Results of the study indicate that a greater number of females responded to the questionnaire. While these results do not indicate that females are most susceptible to DM, respondent bias may be a possible explanation for the greater number of female respondents.

While the gender distribution may be a reflection of the demographic features of patients attending the diabetic clinic, this was not the objective of the study, and may prove to be fruitful for further studies focussing specifically on gender. With this in mind, interesting gender differences are noted in the present study which may provide evidence to earlier research conducted by authors such as Rubin et al and Ward et al[14,61] who report that HRQOL is better among diabetic men than among diabetic women.

The HRQOL in this study resulted in a mean score for males of 216.98 and a mean score of 223.78 for females. These HRQOL scores may indicate that, females may have a reduced QOL in comparison to males. Rubin et al have reported that males are more satisfied with their diabetes treatment regimen, and missed fewer days of work and fewer leisure activities as a result of diabetes, than women.[14, 61] Furthermore, it has been reported that men with diabetes report less disease impact and greater treatment satisfaction than women.[48, 73,61] These results are further consistent with a study conducted, on females in the Netherlands

whereby, women had significantly lower HRQOL scores than men.[28, 74] The differences are explained as being due to gender differences in levels of obesity. The present study, supports these results, as females are found to be more obese in comparison to males, and thus supports the view that obesity may be a factor that affects HRQOL and has an adverse impact on females.[58]

Age as a factor of diabetic patient's QOL produced divergent results. Researchers such as Brown[62, 76], Rubin et al.[14, 61], and Hanninen et al.[77,78] have reported that age has no effect on diabetic patient's QOL; however Gulliford [68, 79], Redekop et al.[28,74] Klein[63, 64] and Glasgow et al[46,68] report that age may have a negative effect on patient's QOL. This was attributed to older people having lower levels of energy, physical activity and social functioning. Results from this study, however indicate that there is no association between age and HRQOL. These results are consistent with Brown, Rubin et al and Hanninen et al.[14,76,77] While an explanation for this could not be found in the literature, this may be indicative that physical health does decline with age; however this may not indicate that older people are physically incapacitated and unenergetic.

5.2 Duration of DM and HRQOL

The duration of DM has been reported by Aalto et all[47] and Connel et al[69] to be associated with a decreased HRQOL. Possible reasons could be that the longer one has DM, more complications could develop thus worsening QOL. Rubin et al.[14], Aalto et al 1997 [47]; Rubin and Peyrot 1999[14]; Redekop et al 2002 [28] found no association between duration of DM and HRQOL which is supported by this study. No explanation for this could be found in the literature. Possible reasons could be that the duration of DM does not necessarily correlate with good control, experience or level of complications, thus not necessarily impacting on QOL.

5.3 Socio-economic status and HRQOL

Connel et all [69] and Franciosi et all [81] report an association between socio-economic status (income and educational level) and HRQOL. Our study measured employment as a socio-economic factor, however no association was found. This may be due to employment status not being a reliable factor to understand an individual's socio-economic status. An individual's employment status does not necessarily reflect on their financial status. Therefore employment status may not have a significant impact on the HRQOL, as is evidenced by no association being found. One also has to be mindful of the fact that the unemployment rates in South Africa are extremely high compared to any first world country.

5.4 Exercise and BMI

Fifty-three percent of respondents reported exercising regularly. The beneficial effects of exercise have been demonstrated in studies including "The Harvard Alumni Study" [31, 26] and "The Insulin Resistance Atherosclerosis Study" [32.] Despite the efforts by clinicians to describe the benefits of exercise to patients, patients still do not heed this advice. While this highlights an important factor, which is outside of the scope of this project, different approaches of highlighting the importance of exercise needs to be communicated to patients and clinicians alike. In reference to this study, the benefits and importance of exercising in control hyperglycaemia and DM are well documented.

Exercise is closely related to weight control, which is reported to be an important controlling factor in the management of diabetes. However, the results indicate that only half of the study population engage in regular exercise, and this may be a function of the age (median age 58 years). It may be plausible to suggest that the older an individual becomes, the more sedentary the lifestyle becomes, thus exasperating the problem of DM and general HRQOL. Furthermore, as an individual ages, physical strength decreases and this may also be further

compounded by diabetes related complications. Patients do not perceive the benefits of exercise to positively impact the QOL, which is further evidenced by the lack of an association between HRQOL and exercise. The study did not use diabetes related complications as a variable, therefore it is beyond the scope of this study to further expand of the effects of physical activity relating to diabetic complications.

Despite a qualified dietician being consulted by all patients at the clinic periodically for dietary advice; 88.60% of patients are overweight and obese. Only 9 patients (9.30%) were in the ideal BMI category (Figure 10). Obesity is associated with a significantly reduced QOL in patients with diabetes. [59] While obesity may be in part linked to a lack of exercise, the socio-economic status linked to the types of foods that patients can access may also be a factor. The WHO reports that individuals from low socio-economic brackets have greater access to energy-dense, nutrient-poor foods, such as refined grains and added sugar. Thus, further research is needed in attempting to implement existing SEMDSA dietary guidelines that factor into socio-economic status and readily available foods, which may assist in addressing part of this problem that has consequences beyond diabetes control.

Andrzej et al [87] and Akinci et al [86] report that BMI affects QOL. However results from the present study provide no evidence for an association between the two, and indicate that BMI and thus weight may only be significant for specific medical conditions, and have no impact on DM. While these conditions may be linked to QOL, patients do not perceive this to be a significant factor in specific reference to DM.

5.5 Hypertension and Dyslipidaemia

The age of the population is skewed to the elderly (60 years and above), therefore the results may not be a reflection of the individuals with high cholesterol and high blood pressure as parameters of variable that impact HRQOL, at the younger age cohorts.

Diabetes and hypertension seem to comparably impair HRQOL.[60] There was an association between HRQOL and concomitant HT and dyslipidaemia. DM and HT have comparable adverse effects on HRQOL.[40]

During the planning stages of this study, a high prevalence of HT and dyslipidemia was anticipated due to the high prevalence of Metabolic Syndrome in the population studied. The prevalence of HT in the present study group was 70% (Figure 7) and that of dyslipidaemia was 52.60% (Figure 8). The combination of DM, HT, dyslipidaemia, in the large number of patients in this study conveys a high risk for cardiovascular disease.

HT is reported to have a negative effect on HRQOL[33], especially when it comes to patient perceived general health, although its impact on HRQOL is usually less contributory than that of other chronic diseases.[33]

Previous studies on the QOL of patients with HT and DM, shows that HT in conjunction with type 2 DM has a deleterious effect on HRQOL. This finding suggests that the earlier detection of co-morbid diseases and the appropriate management of both diseases, not only improves the cardiovascular outcome, but the ability to function well in daily living too.

The present study found an association between HRQOL and HT, as well as HRQOL and dyslipidaemia, thus supporting previous reports of the adverse impact of DM and HT on patient's HRQOL. This may be caused by both conditions imposing similar self-perceived limitations in patient's physical and mental functioning. Another possible explanation could be the added pill burden, side effects of the drugs or the combined dietary restrictions and complications of the diseases.

5.6 Lifestyle

The population studied in this study includes a substantial Muslim community who automatically will not drink due to religious convictions. Religious choice was not accounted for in the questionnaire.

The effects of lifestyle interventions on type 2 DM patients are relatively well described in the literature.[113-115] It has been noted that many lifestyle strategies can reduce the complications of type 2 DM. Lifestyle modification in relation to obesity, eating habits, concurrent cigarette smoking, alcohol consumption and physical exercise can play a major role in the prevention of complications relating to DM. There has been substantial work in the development of behavioural strategies to modify these lifestyle habits. However, these are neither easy to implement nor to maintain on a long term basis. If patients maintain a healthy lifestyle; a balanced healthy diet and exercise regularly, this can lead to considerable benefits for the prevention and control of diabetic complications, particularly for reducing the high cardiovascular risk associated with DM. Healthy lifestyle measures may best be achieved through a holistic, multidisciplinary approach to the management of DM, which includes the use of a dietician, physiotherapist, diabetic counsellors, and support from health care providers, community members and people living with diabetes.[113,114,115,116]

5.7 HRQOL and HBA_{1C}

HbA_{1C} levels are important in determining whether glucose levels are being adequately controlled, and is widely used to determine whether treatment is optimal or needs to be intensified further.

Only 28 patients (14.0%) had a target HbA_{1C} of less than 7%. The vast majority of patients, (40%) had HBA_{1C} levels greater than 10%, which would require additional action to be taken as recommended by the ADA guidelines (Table 11).

This study shows the relationship between HbA_{1C}, a critical clinical biomarker in DM, and the D-39, a patient-centered diabetes-specific QOL measure among type 2 diabetic patients attending the diabetic clinic at HJH.

This result supports the results found by Khanna et al.[42] Several earlier studies have reported on the association between clinical indicators, such as HbA_{1C}, and a variety of diabetes specific QOL measures.[88-95] Carey et al, [97] found weak associations between the two, however Boyer et al [24] found limited evidence to support this. Furthermore, previous studies report on measures that have poor evidence for validity and reliability [90,91,96,97], focus on single aspects of QOL [92,93,97], and overlook essential components of QOL such as physical and social functioning[23], or include several items that are not diabetes-specific.[23] Additionally, several reviews of diabetes-specific QOL [23, 98,99] have recognized the lack of evidence on the responsiveness of QOL to changes in patient's health status.[42] The present study's analysis of HbA_{1C} and diabetes-specific HRQOL may address some of the limitations of previous studies.

5.6 Quality of Life scores

It is important to note that the absolute values (i.e. mean scores) are not of significance. These values can only be used to compare two groups and then deduce which of the groups has a better or worse score (QOL) for the parameter being studied. Five parameters of QOL are analysed by the Diabetes-39 questionnaire viz. Energy and Mobility, Sexual Functioning,

Social Burden, Anxiety and Worry and Diabetes Control. The present study found that sexual function, anxiety and worry and diabetes control impact QOL the most.

Sexual function

According to ADA, sexual dysfunction is one of the most common complications of DM and also one of the most underdiagnosed. Diabetic men are three times as likely to develop erectile dysfunction (ED) as compared to non-diabetic men. The cause is often multifactorial, but most commonly reflects endothelial dysfunction and autonomic neuropathy.[102]

There are many studies showing that sexual dysfunction and in particular, ED negatively affect QOL. The Exploratory Comprehensive Evaluation of Erectile Dysfunction (ExCEED) study reported that in the general population of patients presenting to their urologist, ED negatively affects both general QOL and HRQOL.[100]

In another study from the ExCEED group, Penson et al. made a comparison between erectile function and disease-specific QOL of men with ED and DM, to those of men with ED without DM. They found that those with DM reported significantly worse erectile function and intercourse satisfaction than those without DM. Importantly, the diabetic patients also reported that ED had a considerably worse psychological impact on their overall emotional well-being when compared to their non-diabetic counterparts.[101]

Female Sexual Dysfunction or Disorder is more difficult to define and specific studies in with regard to DM are limited. Problems with arousal, lubrication and orgasmic dysfunction occur, but in general, psychological issues appear to predominate.

The present study found that there is an association between sexual function and HRQOL in type 2 DM, however the study did not compare sexual function between males and females nor did it delve further into the type and extent of sexual dysfunction that the patients encountered.

Clinicians often do not enquire about symptoms of this diabetic complication. This results in considerable under diagnosis because patients are often reluctant or embarrassed to initiate a discussion regarding these issues. In doing so an important and pivotal opportunity is lost where patient's QOL can be improved.

Anxiety and Worry

According to the Canadian Diabetes Association, little is known about the relationship between DM and anxiety.[118] Anxiety disorders seem to be increased in patients with diabetes, when compared with the general population (14 vs. 3 to 4%, respectively). As many as 40% of diabetic patients have at least some anxiety symptoms.[118] Fear of hypoglycaemia is not uncommon in patients with DM. Fear of hypoglycaemia may not affect HRQOL per se (e.g. has little impact on pain or mobility) but it can affect aspects of more general QOL (e.g. independence, ability to work or perform household duties, enjoyment of leisure activities).

Goldney et al conducted a study to assess the prevalence of DM and depression and their association with QOL using a representative population sample. They found that depression

in those with DM is an important co-factor that requires cautious management because of its severe impact on QOL.[105]

Recent studies suggest that anxiety disorders in patients with both type 1 and 2 DM is associated with poor glucose control. This can be extrapolated to a poorer QOL.

Shew WH, et al, found in a study conducted in 2012 that hypoglycaemic symptoms were associated with reduced QOL, as well as increased anxiety and worry in diabetics treated with OHA.[103]

The present study found an association between the anxiety and worry component of HRQOL in type 2 diabetes, irrespective of being treated with insulin alone or with OHA.

Diabetes Control

The never-ending demands of diabetes care, such as watching one's diet, exercising regularly, monitoring blood glucose levels, and scheduling and planning life around one's treatment, affects QOL in patients type 2 DM.[12] One would assume that in addition to improving glucose control and reducing diabetes related complications, improved adherence to a treatment regimen would lead to an improved HRQOL.

However, some studies indicate that engaging in self-management behaviour has a negative effect on QOL.[46, 106-107] In a study conducted by Ken Watkins et al, it was suggested that dietary adherence may negatively affect QOL by increasing the level of perceived diabetes

related burden. People affected by DM are often restricted in the amount, type and timing of food consumed (e.g. glycaemic index of foods, eating mandatory meals at certain times, waiting for insulin effect before eating meals etc.). These restrictions may negatively affect an individual's QOL and their interaction with people around them in their social lives and in the work place.[108]

The present study found an association between a patient with DM and their diabetic control as measured by HBA_{1C} and QOL. The reason is probably multifactorial; ranging from dietary restrictions, to possible deterrent in social events, the time and commitment required in achieving good glycaemic and weight control.

Chapter 6: CONCLUSION

The purpose of this study was to determine whether there is an association between the HRQOL and certain indicators of the severity and control of type 2 diabetes at the Diabetic Clinic at Helen Joseph Hospital.

1. The study showed an association between poor HBA_{1C} and a decrease in HRQOL. The results of this study, which are consistent with international studies, reveal that diabetic patient's glucose control/HBA_{1C} has a significant impact on HRQOL. The treatment of a chronic disease like DM is different from acute illnesses. It requires a multidisciplinary approach with a lot of emphasis being placed on the patients' responsibility for good glucose control. Clinicians should to bear this in mind when treating patients, placing more emphasis on reaching target HBA_{1C} levels as per the ADA guidelines.

2. HT and dyslipidaemia have an association with HRQOL. This finding suggests that the earlier identification and the appropriate management may not only reduce complications but also improve QOL. Considering the high prevalence of HT and dyslipidaemia in type 2 diabetic patients, and its impact on HRQOL, clinicians need to pay more attention to better blood pressure and lipid levels in an attempt to reach target levels. This could be extremely useful, particularly in early treatment of DM and HT, at which point improving outcomes and consequently HRQOL is still possible.

3. The study also found an association between type 2 DM and certain domains of HRQOL. QOL was more affected by sexual functioning, anxiety and worry and diabetes control.

4. There was no association found between HRQOL and other clinical parameters namely; number of insulin units used per day, exercise, BMI, lipogram, and the use of OHA.

5. Demographic parameters; age, gender, age at diagnosis, employment status, living arrangements were also shown to have no impact on HRQOL in this study.

6. There was also no association found between HRQOL in patients who consumed alcohol and cigarettes or in those who didn't.

Considering the high morbidity and mortality rate of DM, clinicians need to consider an array of information when creating a treatment regimen for patients. It is also vital to consider how DM affects each patient's QOL. Various psychological factors need to be considered i.e. mental and physical strain, costs incurred to acquire a medical consultation, days spent away from work, social costs associated with the loss of independence. HRQOL of patients with diabetes need not be lower than its non-diabetic counterparts. Managing DM by controlling glucose levels, blood pressure, cholesterol levels as well as attempting to achieve better psychological aspects of a patient's disease, can lead to an improved HRQOL.

6.1 Limitations of this study

a. English may not be the first language of many of the patients in the sample group therefore the D-39 questionnaire may not accurately reflect the patients QOL.

b. The audited sample is rarely entirely representative of the general population at large. A proportion of type 2 diabetic patients at Helen Joseph Hospital (HJH) are managed at a general Medical Outpatients Clinic. These patients are awaiting appointments or are in the process of being referred to the diabetic clinic. Therefore the results of this study may not be a true reflection of the total diabetic population attending HJH.

c. The data was collected by a single researcher hence the results cannot be validated.

d. There was no control group against which to compare the study group

e. The study represents QOL at a single point in time, therefore it is difficult to determine the change in HRQOL over time

f. The study did not use all the parameters used in previous studies; namely micro and macrovascular complications as these were not documented in all the patients files. It has been shown in the literature that diabetic complications affect a patient's HRQOL. Had this parameter been used, it could have either refuted or concurred with the literature.

g. The study did not distinguish between the number of times a patient injected themselves. This may be an important aspect impacting on patient's HRQOL and it is recommended to be used as a variable in future studies.

6.2 Strengths of this study

a. All the patients have been reviewed by physicians since the first time they attended the clinic.

b. The blood results are standardised and are obtained from the same laboratory (National Health Laboratory Service).

c. The data was collected from patients' records by a single researcher only. This ensured that the data was collected in a standardised manner and is reliable.

6.3 Future studies

Future studies may collect QOL data both before, and after self-care educational programs are implemented with patients, so that the effect of QOL measures can be better assessed. The inclusion of a control group that does not receive any programs beyond routine healthcare may also allow for future assessment on the impact on patient's HRQOL. A lot more research needs to be done using diabetes specific QOL assessments in future, especially in South Africa, considering the paucity of information regarding this subject.

More studies are needed to confirm or refute the findings of this study. It is recommended that this study to be repeated in clinics dealing with patients from the other socio-economic backgrounds in the community.

It would be interesting to note if there is any male to female difference in HRQOL in each parameter studied. This would either confirm or refute previous studies done.

Future studies could include socio-economic status (income and education level) as a parameter affecting HRQOL in diabetic patients. Furthermore if a person is employed, the study could delve further into the type of work done and thus determine if work influences a patient's QOL, in terms of finances, stigma of diabetes at work, sick days off etc.

Many previous studies included micro and marcovascular complications as a parameter when determining HRQOL. Unfortunately it was not logistically possible in this study, due to the lack of data in files. It would be recommended for future studies to include this parameter.

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