MASTER THESIS

UNIVERSITY OF BERGEN

Department of Clinical Science

"Nutritional and clinical status of patients with diabetes in Zanzibar: A clinical follow up study"

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Master's programme in Human nutrition

June 2020

Acknowledgement

To my supervisor, Professor Ingunn Marie S.Engebretsen, your dedication and passion for your field and students is truly inspirational. Thank you for always guiding me in the right direction with this thesis, your constructive feedback, and for all the time you have put into this study.

To my co-supervisor, Dr. Elinor M. Chelsom Vogt, thank you for giving the opportunity to write this thesis and for trusting me to follow up on your original study. And thank you for all the constructive feedback you have given me.

I would also like to express my deepest gratitude to all of the highly professional personnel at diabetic clinic in Mnazi Mmoja hospital, Dr. Faiza, nurse Mwanaharusi and Dr. Ali Hussein; this study would have been impossible without your effort, positive mindset and dedication.

Thank you to professor Eirik Softeland, for your important insights on this study.

To my dear mother, my father and sister, your unconditional love and encouragement kept me going to the end of this thesis.

Finally, to my lovely husband, Mohammed, your strategic mind, patience and support was more than I could I ask for to get me through this time.

Abstract

Background

Diabetes mellitus is on the rise in Sub-Saharan Africa. On the island of Zanzibar food habits and nutritional status among diabetes type 2 patients is not well described. Rising food prices accompanied by limited health resources, are factors risk for developing diabetes complications.

Objectives

Investigate nutritional and health related factors of a cohort of patients with diabetes type 2 in Zanzibar.

Method

Follow up of an existing cohort of 100 diabetic patients from 2015 attending the diabetic clinic in Mnazi Mmoja Hospital.14 patients were deceased, 24 were lost to follow up, and 62 patients were tracked of whom, 2 patients were not eligible for inclusion, thus a total of 60 patients were included in the follow up study. Food frequency questionnaire (FFQ), body mass index (BMI), blood pressure, laboratory assessments of metabolic status and case report form on diabetes complication were collected of 60 patients. Point of care instruments were used on site. Logistic and linear regression model were used to investigate association between predicted variables and outcome variables.

Results

Thirty-three men and twenty- seven women were included, with mean age of 55 years. Mean Hba1c was 9.5% and fasting glucose 12.3mmol/L. Slightly raised LDL profile was found in the population, mean 3.0mmol/L. Hypertension was observed in more than half of the population. In accordance with poor metabolic control, diabetes complications were rampant. FFQ results showed a high consumption frequency of refined carbohydrates, food rich in saturated fatty, and a low consumption of vegetables. Positive association was observed for the duration of diabetes and number of foot ulcers.

Conclusion

The nutritional and health factors investigated suggest a population with poor diabetes management as evident by the metabolic and diet assessments. There is no improvement in HbA1c or blood pressure since the assessment in 2015 and the reported number of diabetes complications have increased.

1 TABLE OF CONTENT

Abstract........3
List of Tables........6
List of Figures........7
Abbreviation........8
Introduction........9
1.1 Prevalence of Diabetes mellitus........9
1.2 Diabetes mellitus and pathophysiology........10
1.2.1 Diabetes mellitus type 2........11
1.2.2 Impaired glucose tolerance (IGT)........11
1.2.3 Environmental and genetic factors linked with developing diabetes type 2........12
1.2.4 Diagnostic criteria of diabetes mellitus type 2........12
1.2.5 Complications........13
1.3 Diabetes-nutrition and lifestyle........13
1.3.1 Exercise........15
1.4 Research and nutritional assessments........15
1.4.1 Dietary assessments........15
1.5 Diabetes and nutrition on the island of Zanzibar........16
1.5.1 Trends and prevalence of diabetes mellitus in Zanzibar........16
1.5.2 Nutrition in Zanzibar........16
1.5.3 Diabetes care in Zanzibar........17
2 Study rationale........19
2.1 objectives........20
2.1.1 General objectives........20
2.1.2 Specific objectives........20
3 Material and Method........21
3.1 Study design and place........21
3.2 Population........21
3.3 Participants and recruitment........21
3.4 Follow-up procedures........24
3.5 Method prior to data collection........25
3.6 Methods for blood sampling and analysis........26
3.7 Data management........26

3.7.1 Data analysis 27
3.7.2 Handling of missing values 27
3.8 Ethics 28
4 RESULTS 30
4.1 Socio-economic characteristics of study population 30
4.2 Clinical characteristics and medication use 31
4.3 Anthropometric and metabolic status 33
4.4 Dietary patterns 34
4.5 Individual diet diversity scores 39
4.6 Association between metabolic status, dietary patterns, socio-economy, and neuromuscular symptoms 41
4.6.1 Association between duration of diabetes, health and nutrition. 42
5 Discussion 43
5.1 Discussion of findings 43
5.1.1 Discussion of the linear regression and the logistic analysis 46
5.2 Discussion of methods 47
5.2.1 Limitation of food frequency recall 48
5.2.2 Limitation of analytical instruments 48
5.3 Conclusion 48
6 References 49
Appendix

List of Tables

Table 1a Socio-economic characteristics of study population, continuous variables…….. 22

Table 1b Socio-economic characteristics of study population, categorical variables………23

Table 2 Clinical diagnosis and medication use……………………………………………...24

Table 3 Anthropometric and metabolic data of study population…………………………..25

Table 4 Semiquantitative food frequency questionnaire results…………………………....27

Table 5 Semiquantitative food frequency report of specific local dishes……………….....29

Table 6 Individual diet diversity score of study population………………………………..31

Table 7, Mean and Median values of the individual diet diversity score………………………………………………………………………………..31

Table 8 Aggregation of food groups from the Food Frequency Questionnaire to create Individual dietary diversity score………………………………………………………...32

Table 9, overview of a crude regression and adjusted analysis with HbA1c as the Response variable…..…………………………………………………………………….33

Table 10 logistic regression analysis of duration of diabetes, health and lifestyle…………35

List of Figures

Figure 1 Overview of the current prevalence and estimated prevalence of diabetes mellitus type 2……………………………………………………………………………………..8

Figure 2 Map of the Island of Tanzania ………………...…………………………………15

Figure 3 Flow chart of study participants ……………………………………………….22

Figure 4 Utensils used during data collection to record approximate serving size ………..24

Figure 5 Overview of the total number of patient results (n) included in the descriptive data……………………………………………………………………………………28

Abbreviations

WHO- World Health Organization

SSA-Sub Saharan Africa

FFQ- Food Frequency questionnaire

CVA- Cerebrovascular accidents

LDL- low density lipoproteins

HDL- high density lipoproteins

IGT- Impaired glucose tolerance

OGTT- Oral glucose tolerance test

Introduction

Non-communicable diseases (NCD's) – cardiovascular disease, cancer, chronic respiratory diseases, and diabetes are rising globally. Thirty-six million individuals die of NCD's each year, which is equivalent to 63% of the global deaths [1]. Sub-Saharan Africa (SSA) are experiencing a demographic transition with changes in patterns of diseases, while infectious disease was rampant earlier, NCD's are now increasing [2]. In 2004, 25% of all the deaths in SSA were caused by NCD's. [3] Diabetes mellitus is one of the most common NCD in low - and middle income countries, and the major reasons are population ageing, economic development, urbanization, unhealthy eating habits and sedentary lifestyle [4].

1.1 Prevalence of Diabetes mellitus

Diabetes mellitus is the ninth major cause of death globally, and numbers have quadrupled in the past three decades [4]. In 2014 the number of patients that were diagnosed with diabetes was 422 million and in 2016, 1.6 million deaths were directly caused by diabetes. By 2045 the number of diabetes cases are expected to increase by 48% compared to 2019 (Figure 1). It is estimated that almost 50% of individuals that are effected by diabetes are unaware that they have the condition [5].

In 2010, 12.1 million individuals were living with diabetes in Africa, and there is evidence that this is an increasing trend. [6]. The prevalence of diabetes reaches up to 16% in some Sub-Saharan countries [3].

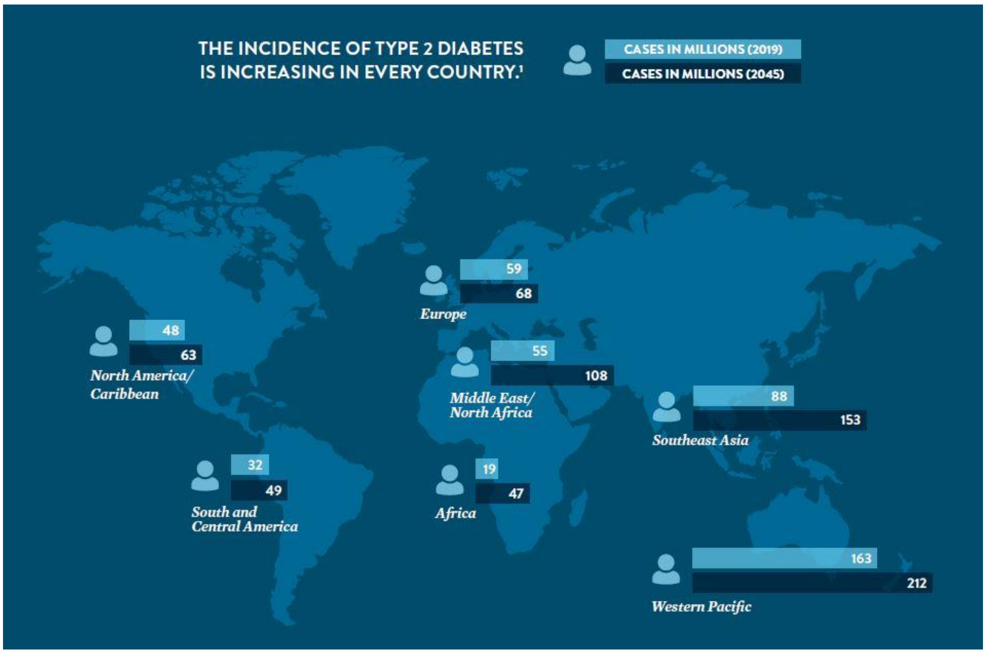

Figure 1 Overview of the current prevalence and estimated prevalence of diabetes mellitus type 2. International Diabetes Federation. IDF Diabetes Atlas, 9th edn. 2019. Brussels, Belgium. Edited and modified by Abbot diagnostics [5, 7]

In the United Republic of Tanzania an increasing trend of diabetes cases is also observed, from 2.7% in 2010 to 5.7% in 2019 [8].

Eighty percent of diabetes related deaths occurred in low-and middle-income countries [9], considering the relatively young population of most low-income countries this trend indicates that the epidemic is causing premature deaths in these populations. Diabetic neuropathy affects 40 to 60 million people with diabetes globally.

Data from sub-Saharan Africa suggest that large proportions of need for diabetes care and diagnosis are unmet. Including access to screening for complications, counselling and medicines [10].
Many low-income countries have an already overloaded health care system and multiple competing health care issues[5]. Lack of proper education, health care professionals and health clinics, puts patients at great risk of developing diabetic complications. Preventive work is costly, and some countries also rely on international aid to conduct screenings and education.

1.2 DIABETES MELLITUS AND PATHOPHYSIOLOGY

The World Health Organization (WHO) defines diabetes mellitus as a set of syndromes *"characterized by hyperglycaemia and disturbance of the carbohydrate metabolism that are associated with absolute or relative deficiencies in insulin action and- /or insulin secretion". (WHO)* Several subgroups of diabetes mellitus have been identified. The most prevalent are type 1, diabetes type 2 and gestational diabetes. Diabetes type 2 is twenty times more common than type 1 diabetes, with almost 90% of patients having diabetes type 2 and approximately 10% diabetes type 1. [11]

Diabetes type 1 is an autoimmune T-cell mediates destruction of the insulin producing Beta cells in the pancreas, resulting in absolute deficiency in production of insulin. Diabetes type 1 is often diagnosed in young age. [12]

Diabetes type 1 is challenging to diagnose without sophisticated laboratory equipment such as autoantibody testing, therefore there is no exact data on the prevalence of diabetes type 1.Studies has shown that genetic factors are strongly influential along with environmental factors such as viral infections and gut flora [13].

1.2.1 Diabetes mellitus type 2

Diabetes melltitus type 2 is a metabolic disorder where insulin resistance and Beta cell dysfunction are pathological defects. Glucose is the primary stimulus for insulin secretion. Insulin and glucagon serve a counter-regulatory role and are the main controlling hormones in the glucose haemostasis [14]. Insulin secretion depends on the type and physical form of carbohydrate that is consumed, this association is explained further in the chapter about diabetes-nutrition and lifestyle. Diets that are high in certain carbohydrates stimulate more insulin secretion, and may over time result in hyperinsulinemia and subsequent insulin resistance[15]

Insulin resistance is when the target peripheral tissue has a decreased biological respond to the insulin that is produced by the beta cells [12].

The increasing demand of insulin and chronic hyperglycaemia, due to the decreased biological response of the target tissue, results in a progressive loss of beta cell function. The defect in the beta cell function is due to loss of glucose-induced insulin release and is called glucotoxicity. The extent of the Beta cell dysfunction correlates with both glucose concentration and the duration of hyperglycaemia[16]. Insufficient insulin response results in the characteristic state of hyperglycaemia that is seen in individuals with diabetes mellitus.

1.2.2 Impaired glucose tolerance (IGT)

The World Health Organization defines IGT as normal fasting blood sugar levels (<7mmol/L) with elevated plasma glucose response (≥7.8 mmol/L and <11.1 mmol/L) during the oral glucose tolerant test (OGTT) [17]. The OGTT is a test that consist of measuring fasting glucose levels, followed by an ingestion of 75g glucose load within 30 minutes, and a final plasma glucose measurement two hours after ingestion of the glucose load. Impaired glucose intolerance is not a clinical entity, but rather a risk factor before the onset of diabetes mellitus type 2, where elevated blood sugar levels is observed, but without clinical symptoms. Its more rampant among women and is often seen in African and Asian population [17]. In most population studies, up to 60% of people who developed diabetes had impaired glucose tolerance or impaired fasting glucose five years before symptoms occurred. WHO recognizes that impaired glucose tolerance could progress to diabetes mellitus, although 40% revert to normal blood sugar levels [18].

Understanding if a patient has impaired glucose tolerance is crucial, as studies has shown that lifestyle interventions are highly effective in preventing or delaying the onset of diabetes in these patients [18].

1.2.3 Environmental and genetic factors linked with developing diabetes type 2

Diabetes type 2 has a multifactorial ethology, with contributions from obesity, genetics and lifestyle [19]. The metabolic condition is ten times more likely to occur in an obese individual with a parent who has diabetes, compared to an individual with no history of diabetes in the family [16]. Studies have also shown that genetics linked to different ethnicities might be of significance in developing insulin resistance [20].

Inadequate physical activity and diet high in carbohydrate and fat lead to excess energy input to the body that is stored as glycogen and lipids. Over time this can lead to increased risk of metabolic disorders [16].

In a cohort study of 18,320 same-sex twin, the risk of type 2 diabetes increased with decreasing birth weight. Twins with birth weight of less than 2000 grams had a 2-fold increase in risk of diabetes type 2 [21]. The study also showed that genetic mechanism behind the development in diabetes type 2 in adulthood played a central role in this association.

The association between low birth weight and diabetes mellitus has led to speculation that loss of beta cell function could be a consequence from a disturbance in the beta cell neogenesis, that occurs preterm in humans, thus affecting the development of the pancreas in the onset of adulthood [22].

1.2.4 Diagnostic criteria of diabetes mellitus type 2

The WHO recommends performing a fasting plasma glucose test where values of glucose above ≥7mmol/l (126mg/dl) or 2-hour plasma glucose ≥11.1 mmol/l (200mg/dl) are diagnostic of diabetes. The tests should be repeated on a different day. HbA1c testing is not considered suitable for diagnostic purpose due to the lack of global standardisation and other influencing factors such as anaemia and hemoglobinopathies. HbA1c is rather important in monitoring long-term glucose levels and patients’ responses to medication type and dosage [17].

1.2.5 Complications

Diabetes is a progressive disorder, and if poorly monitored it leads to increased risk of developing long term microvascular complications such as retinopathy, renal failure, as well as microvascular diseases and neuropathy. Patients with diabetes are often prone to communicable diseases such as pneumonia, bacteraemia and other NCD such as cardiovascular diseases [23]. A population based cohort study has shown a significant relationship between elevated blood sugar levels and acute myocardial infarction [24].

Diabetes is the leading cause of kidney failure, causing patients to undergo a lifetime treatment with dialysis, if available or more severe outcomes including death in low resource settings. Most of the damage observed in the microvascular level are caused by accumulation of sugar in the blood [16].

Polyneuropathy is a symptom that is causes by demyelinisation of nerve cells, causing nerve signals to slowly weaken, leading to loss of sensation in the limbs. Polyneuropathy together with macrovascular reduction of circulation in the limbs increase the risk of ulcers and infections [5].

Foot ulceration may lead to lower limbs amputation. Diabetic foot ulcers are a major cause of hospital admissions. In some cultures, patients that are not used to wearing footwear might develop severe ulcers and if left untreated without proper health facilities it could lead to amputation. From the year 1999-2011 the five year mortality proportion of patients with diabetes varied from 5-57% in Sub-Saharan Africa [23].

A prospective cohort study of diabetic patients in Muhimbili hospital in Tanzania, confirmed that 70% of lower limb amputation occur in patients with diabetes, and the mortality associated with foot ulcer is reported to be 50% [25].

1.3 Diabetes-nutrition and lifestyle

The risk of diabetic complications are strongly associated with hyperglycaemia [26], and a reduction in HbA1c reduces the risk of complications. Diabetes related nutritional knowledge is a crucial tool for patients to self-monitor and achieve favourable glycaemic control and combat potential complications [27]. Diet should be individualized as any other medical treatment, to motivate individuals with diabetes to achieve glycaemic control. Usual food habits, treatment goals and desired outcomes should be taken into consideration.

The blood glucose haemostasis is strictly regulated by the body, and is the most important energy source for most human cells. An important interaction between the hormones insulin and glucagon prevents the body from falling into hyperglycaemia and hypoglycaemia.

In controlling the haemostasis of blood sugar, insulin release, obesity, and weight loss, the rate at which glucose is absorbed by the intestinal tract appears to be important [28]. After ingestion of a carbohydrate-containing food the blood glucose concentration changes, and this is called the glycaemic response of the food. Glycaemic index (GI) is a term used to classify dietary carbohydrates that induce a glycaemic response.
Refined starchy foods have a high GI score, while non starchy vegetables, fruit and legumes tend to have a low GI score.

Food utilization is an important factor that can change the GI of food [28]. For example, the GI of a baked potato is higher than an instant mashed potato. When evaluating the GI content of food it is also important to understand the glycaemic load (GL), which is the average weighted GI of food multiplied by the percentage of dietary energy as carbohydrate [15]. The carbohydrate in a carrot has high GI score, but the GL for a carrot is low, because it contains a small amount of carbohydrates in grams. Therefore food that is high in GL gives a greater elevation in the blood glucose and greater insulinogenic effect of the food [28].

Diets high in glycaemic index, induce a rapid rise followed by a fast drop in glucose levels and give a false sensation of hunger, and might cause overconsumption of food [15]. High GL food also stimulates more insulin secretion. Patients with diabetes mellitus should limit the intake of food that are high in GL, as it may cause unregulated diabetes. Studies have shown a association between long-term consumption of diets with high GL and the risk of obesity, type 2 diabetes and cardiovascular diseases [29, 30].

Advice on diet and lifestyle are an important of the treatment of type 2 diabetes [31]. Nutritional advice is individualized, and may consist of caloric restrictions if the patient is overweight, restriction on saturated fatty acid intake, and high unrefined carbohydrate content. There is evidence that the amount of carbohydrate in meals are more important the source. Dietary fibre intake above 50g/day may have beneficial effect on glycaemia, insulinaeima and lipemia [32]. There is also evidence that obese patients with diabetes type 2 have increased turnover of proteins, therefore increase in protein intake is favourable, if the patients are not suffering from renal failure.

1.3.1 Exercise

Exercise is proved beneficial for its effect on hyperglycaemia and reduction in free fatty acids [32]. Skeletal muscles demand for fuel molecules such as glucose increases drastically as muscle contraction increases [28]. In type 2 diabetes, exercise seem to increase the peripheral glucose uptake, by increasing the glucose transporter 4 (GLUT4) translocation on the skeletal muscle cell surface [33]. This reaction decreases the insulin secretion and makes muscle cells take up large amounts of glucose to produce ATP. Positive outcomes have also been observed in relation with reducing stress and the feeling of wellbeing.

1.4 RESEARCH AND NUTRITIONAL ASSESSMENTS

Nutritional assessments can be defined as *"the interpretation of information from dietary, laboratory, anthropometric and clinical studies"* [34].

The combination of these assessments provide information of the nutritional status of individuals or population groups, and provide information about utilization of nutrients [34]. It is also used to evaluate, and monitor the effect of nutritional interventions.

1.4.1 Dietary assessments

There are three widely used dietary assessments to understand nutritional deficiencies, estimate nutrients intake and identify consumption frequency; Food record, 24 hour recall, and Food frequency questionnaire (FFQ) [35].

Food record requires individuals to record the food and beverages intake with amounts, over one or two days. It requires motivated individuals and high literacy [35].

The 24 hour recall is a retrospective method that asks individuals food and beverages consumed the past 24 hours [35]. It requires a skilled interviewer to ask in a way to retain memory and details of how the food was prepared by individuals. It collects information about one single day, and should therefore be repeated on a separate day to capture usual eating habits.

The food frequency report provides information about usual intake over a long period of time. The FFQ could be made semiquantitative if information about approximate amount of portion size is collected [34].

In a low resource setting the FFQ requires an interviewer or a trained nutritionist or nutritional educator to establish a understanding of the meaning of the food groups presented. A food composition table with information about usual eating habits and food types of the country is important to capture the right types of food that are being consumed and to calculate nutritional values.

1.5 DIABETES AND NUTRITION ON THE ISLAND OF ZANZIBAR

Zanzibar is a semiautonomous Island and part of the United Republic of Tanzania. The Island is located in Sub-Saharan Africa, and consists of two major islands, Unguja and Pemba.

The demographics and culture in Zanzibar are a consequence of its geographical position in the Indian ocean. Serving as an important trade centre for centuries has resulted in immigration, transmigration and conquest by European and Arabic countries.

The ethnic characteristics of most the Zanzibarian population is a result from cross-cultural and ethnic-marriages, making the island unique and significantly different in culture and demographic characteristics from most African countries [37]. The dominating ethnic groups are Shirazi, Arab and Swahili.

Figure 2, Map of the Island of Zanzibar[36]

1.5.1 Trends and prevalence of diabetes mellitus in Zanzibar

Scarce data is available on the epidemiology of diabetes mellitus in Zanzibar. However, the following is known:

Diabetes mellitus have increased from 17.6% in 2007 to 18.1% in 2008 [38]. Trend of admission from the male and female medical wards in Mnazi Mmoja show that from 2014-2018, diabetes mellitus related admission has increased with 10%. Data from the male surgical ward in Mnazi Mmoja showed that 25 patients were admitted due to diabetic related ulcer in the lower limbs from the period November 2019 to mid-December 2019, some of them with severe outcomes such as septic wounds.

1.5.2 Nutrition in Zanzibar

There are few research articles to be found on the current NCD status, nutritional status and agricultural practise in Zanzibar.

Data from governmental reports indicate that cereals is the most utilized food group in Zanzibar, and account for 56% of caloric intake and 54% of protein intake. Rice and wheat are more consumed now than before and is slowly replacing staples such as cassava and plantain. Cassava and plantain are the second and third most consumed crops in Zanzibar [39]. Legumes and nuts are also important part of the diet and represents 3.8% of caloric intake and 8.6% of the protein intake. Vegetable products are widely consumed, and common vegetables that are cultivated locally are tomato, egg plant, spinach, green pepper, and okra [39]. Fish is the main source of animal protein, meat consumption is low, due to its significant high price compared to fish.

There is no structured food storage facility in Zanzibar, and post-harvest loss is a recognized problem. Fourty one percent of the food requirements such as, fruits and vegetables, in Zanzibar are imported from Tanzania mainland [39]. The agricultural sector of Zanzibar is small scale, and cultivation included crops such as cassava, plantain, sweet banana, mango and some tropical fruits and vegetables. There are some villages in the north of the island that have seaweed farming activities for oversees export. The food prices have been on a steady rise due to the pressing tourism industry, causing low food availability for a large number of the population. Small scale farmers hardly benefit from the tourism industry, as 80% of vegetables and 20% of the fruits that are supplied to hotels are from Tanzanian mainland[39].

14% of the Zanzibari population are under the category "severe food insecure" during the drought season from July to September [40]. Similarly, food that is rich in carbohydrate and fat is becoming easier to access than protein rich foods. The price of a bread bun is approximately 10 TZS and, the price of one egg is 150 TZS. The price difference between carbohydrate dense food and protein rich foods is approximately tenfold, which matter a lot for food availability in low socio-economic settings.

1.5.3 Diabetes care in Zanzibar

Mnazi Mmoja is the only referral and teaching hospital in Zanzibar and serves both Unguja and Pemba. The diabetic clinic in Mnazi Mmoja hospital treats 500 patients each month. The hospital has one certified endocrinologist and one diabetologist. Dietician and certified nutritional educators are lacking in Mnazi Mmoja and other primary and secondary health clinics.

Every three months patients are encouraged to meet at the clinic to report on symptoms, fasting glucose levels and medication usage. The government provides free insulin for all patients and this is distributed through the clinic. Diabetic complications are referred to medical wards, surgical wards and if serious, the intensive care unit. Two smaller diabetic clinics (Kivunge and Makunduchi) are established in the north and south of the Island, and provide basic check-up of the patients, and any complex cases are referred to Mnazi Mmoja hospital.

With limited resources, and few diabetic specialised health care professionals optimal diabetic care is challenging to achieve for patients in Zanzibar. A multidisciplinary treatment with endocrinologist, ophthalmologist, nephrologist, vascular surgeons, physical therapist, nutritionist, and diabetic educators has shown to result in 50% reduction in lower limb-amputation [41].

Clinical laboratory and pre-analytical factors are important in diabetic care [16].
The laboratory in Mnazi Mmoja does not provide plasma glucose measurements, HbA1c testing or lipid profile measurements. Some patients have a glucometer at home, but the cost of 50 strips can be up to 15.000 Tanzanians shillings, equivalent to 5USD, which limits the use.

Without proper clinical and laboratory service, follow up by diabetes specialized health care professionals, nutritional guidance and research facilities, the health and metabolic status of diabetes patients in Zanzibar is unknown. Thus they may be in great risk of developing lifelong morbidity and excess mortality of a relatively young population.

2 STUDY RATIONALE

WHOs non communicable diseases target is to half the prevalence of diabetes worldwide by 2025. The increasing trend of diabetes cases worldwide makes this target hard to reach unless urgent actions are put in place. More research and support needs to be conducted regarding diet habits. This includes understanding and exploring risk behaviour among diabetes patients. The information gained under a diet assessment, combined with biochemical and anthropometric measurements of patients, can give an indication of characteristics and factors associated with severity of diabetes such as hypertension, dyslipidaemia and neuromuscular symptoms. Also, patients need to understand their own dietary habits and how this affects the glucose homeostasis.

Given the importance of improving the nutritional behaviour and the clinical status of diabetes status, and the Haukeland-Zanzibari collaboration opportunities to follow up diabetes patients in Zanzibar we aim to follow up the diabetes cohort from 2015 in order to evaluate the metabolic status as well as the impact of neuropathy on diabetic foot complications and mortality. Further, a dietary assessment as well as of this well-characterized cohort can contribute to greater understanding of their nutritional intake and how that is associated with the metabolic status in DM patients. Further, it will inform clinicians about nutritional habits which can be improved for future glycaemic control through dietary adjustments.

2.1 OBJECTIVES

2.1.1 General objectives

- The aim of the study is to investigate the nutritional and health related factors of diabetic patients in Zanzibar. The factors include socio-economic, dietary, anthropometric, biochemical and clinical aspects.

2.1.2 Specific objectives

- Describe dietary habits of diabetic patients attending a diabetes clinic registered in Zanzibar.
- To assess self-reported common diabetic complications in the same populations.
- To assess the metabolic status of this diabetic population by measurement of anthropometric data (weight/height), biochemical evaluation, of glucose status and cholesterol levels, and blood pressure levels.
- To assess socio-economic, clinical and nutritional factors associated with high glucose levels.

3 MATERIAL AND METHOD

3.1 STUDY DESIGN AND PLACE

This was a descriptive clinical cohort study initiated in Zanzibar in 2014, with 100 patients recruited into the cohort, data that went into this master thesis was a 5-year follow-up with data collection going on from October 25, 2019 to December 3, 2019.

3.2 POPULATION

The patients were recruited in the diabetic outpatients' clinics at Mnazi Mmoja Hospital, Zanzibar. Inclusion criteria were patients with previously diagnosed diabetes. Exclusion criteria were if patients were severely ill or unwilling to participate. Formal statistical power analyses was not feasible, due to the study's observational nature and due to this being a follow-up of an existing cohort.

The first data collection included the assessment of diabetic polyneuropathy in Zanzibar. Fifty-one male and forty-nine female with diabetes were included in the study. The age distribution was ranging from 29-85 years, with the mean age being 54 years. Ninety patients had diabetes mellitus type 2, and 10 patients had clinically verified diabetes mellitus type 1.

3.3 PARTICIPANTS AND RECRUITMENT

The study received approval from the Zanzibar regional ethical committee on October 21, 2019.

In November/December 2019, the same cohort population was contacted through telephone calls and invited for a 5-year follow. Participants met at the diabetic outpatient clinic in Mnazi Mmoja hospital for informed consent and study participation. The study nurse or study doctor contacted the patients by telephone in the native Swahili language. The study participants were continuously called one to two days in advance for six weeks.

The inclusion and tracking procedure was recorded in an excel file. When a participant was not reachable, it was noted and left for further investigations. The study group scheduled an extra tracking day November 22, 2019. All the patients who were not reachable was called twice, and this was done at the diabetic clinic, Mnazi Mmoja Hospital. An updated list of participants that was not traceable was given to the study nurse to discuss with other colleagues if they recognized any participants.

The diabetic clinic staff confirmed 10 participants were deceased, these were not confirmed dead by a death certificate, but nurses recognized the names of the participants. The other four were confirmed dead by close family members.

The study group conducted another tracking day December 6- 2019, in a final attempt to access the remaining 24 that were lost to follow up. Two of the main three diabetic clinics were visited, these were in Makunduchi hospital in southern Zanzibar and Kivunge hospital in northern Zanzibar. Both hospitals had a manual registration of diabetic patients attending the clinic. No names matched our participants' list. The two clinics did not record patients' contact details other than the name, gender, and age.

Out of 24 patients that were lost for follow up, 14 patients did not have any phone record from the baseline study, and ten patients had a record of the phone number, but the number was no longer in use. A total of 60 participants was included in this follow up study, which is equivalent to a participation rate of 60%.

The contacted patients were informed that the study included a questionnaire about socio-economic status, dietary habits, and clinical symptoms, anthropometric measurements, biochemical assessment of metabolic status, and clinical case report form of general health status.

During this cohort study it was very clear that the population where not sensitized to the term research. The study team had to make an effort for each study participant to create a safe environment to limit biased answers.

Upon arrival at Mnazi Mmoja hospital, the inclusion was conducted when the participant had read and signed the consent form. Participants who were illiterate were orally explained the study's procedures and asked to consent with fingerprints. Figure 3 provides details on the study flow chart.

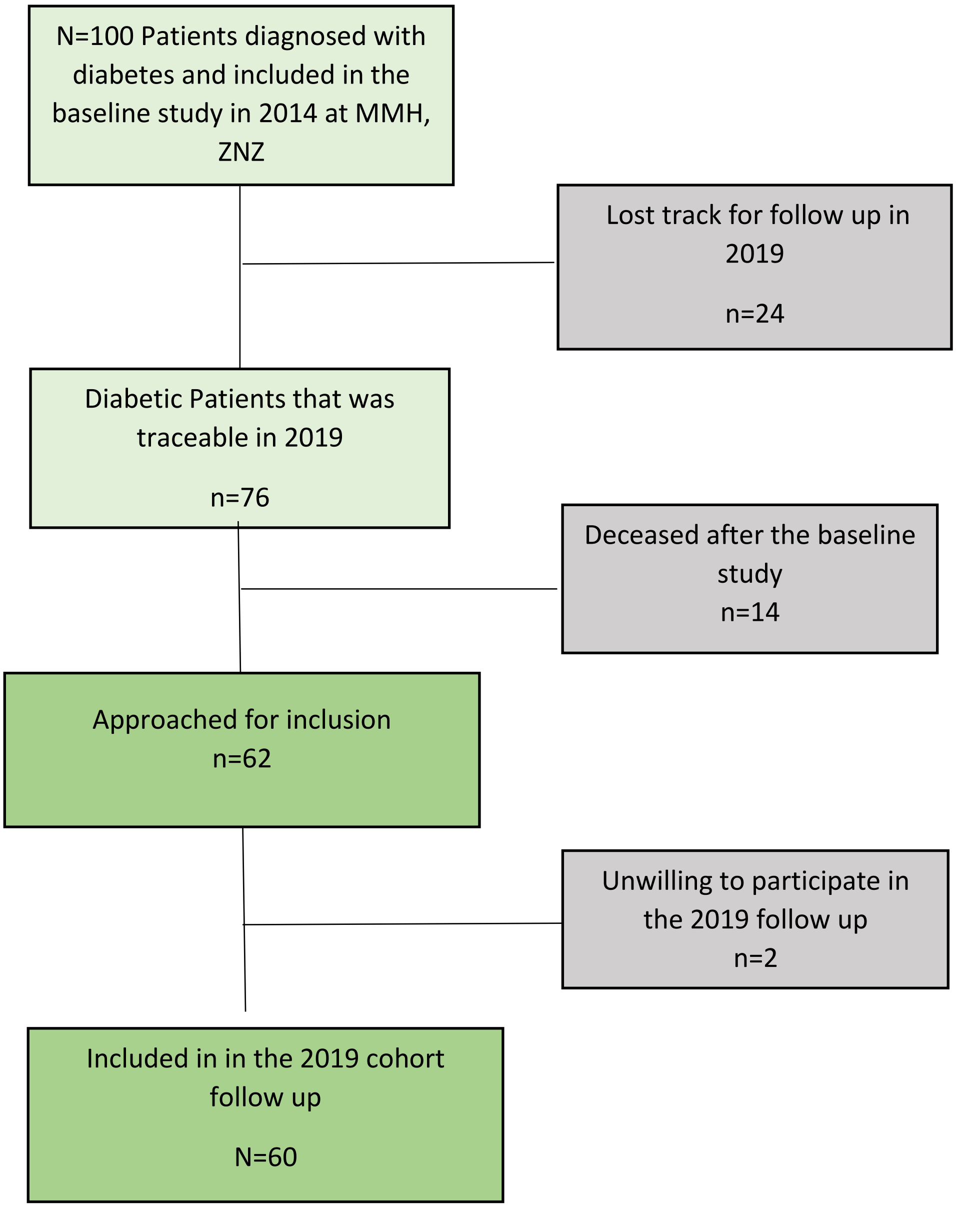

Figure 3 Flowchart of included study participants

MMH, Mnazi Mmoja Hospital. ZNZ, Zanzibar from 2014-2019

3.4 Follow-up procedures

A unique participant ID was used to give opportunities for later merging of the results. However, with a 40% drop-out, we agreed to focus the analysis for this master-presentation on the follow-up study from 2019.

The data collection was an ongoing process, where four patients were invited daily to meet at the diabetes clinic at 8.am. A fasting capillary blood sample was collected on arrival, followed by a venous sample. Capillary samples were taken approximately the same time for the majority of the patients, to avoid biased interruption from the breakdown of glycogen, in cases where participants had entered fasting state. After that, participants went to the interview room where weight, height and blood pressure were recorded according to written standard operating procedures (SOPs). In a situation where participants felt worried or anxious, blood pressure was measured twice.

After that, participants were interviewed using the questionnaire.

Patients who had any abnormal values and who reported that they were not feeling well, were referred to the diabetic clinic for further medical investigation the same day. Laboratory results were recorded in a patients' notebook, as there is no electronic registry at MMH.

The diabetic clinic had assigned a study doctor and study nurse to participate in the study procedure, including recruitment, tool translation, interviews and clinical procedures. The study doctor filled the case report form for the first 10 participants. The study nurse continued filling case report forms for the next 50 after being trained by the study doctor on how to fill in case report forms. The study nurse was supervised during the first two case report forms she filled in.

All blood samples were analysed at the site continuously. Results were written on the specified form before the study participant left the site. Quality control and maintenance of analytical instruments were preformed according to recommendations from the supplier and as needed.

Before the participants left the site, compensation for the waiting time, and transport cost was provided. Each participant was given 5000 Tanzanian Shilling. To ensure stable blood sugar levels after collection of fasting capillary blood samples, participants received a bottle of 500 ml water and a large pack of peanuts. Participants with allergies were allowed to buy something from the hospital café.

3.5 Method prior to data collection

A food frequency questionnaire (FFQ) was used to capture the variety of the diet, such as different types of vegetables, fruits, legumes, meat, and poultry products, but with an emphasis on high food intake in fat, simple carbohydrates and sugars.

The FFQ was designed based on the self-administered semiquantitative FFQ from Block et.al, listed on the second edition of principles of nutritional assessment[34, 42]. The questionnaire was modified to include a list of a total of 59 food items. Also, 17 food recipes were added, from typically consumed foods in Zanzibar to cross-check with the list of regular Tanzanian diet. All questionnaires are available in appendix A1.

The frequency of food intake was captured using five answer options ranging from "daily-weekly-monthly-yearly-never." To capture approximate serving size, three quantity options; "small, medium, or large" were listed on the FFQ. Standardized cups, bowls, and plates were identified and used with reference to the *Tanzanian food composition table.*[43] A visit to local shops that sold cutleries also helped us identify usual portions sizes for a Zanzibarian household.

Figure 4 Utensils that was used during data collection to record approximate serving size.
Study participants was asked to point on utensils that visualized usual portion. From the right is a small-sized plate, medium-sized plate, and large plate. From the left in the back is a large bowl, small bowl, medium-sized cup, and a medium-sized glass

Before data collection, the study nurse translated the questionnaires on socio-economic status and FFQ to Swahili. The questionnaires were printed, and the interviews were similar for all participants. The study nurse first asked the questions in Swahili, then study participants answered in Swahili, and the nurse translated what was reported back by participants, and the master student recorded this in English.

3.6 Methods for blood sampling and analysis

SOPs for blood collection, analysis of samples on Afinion Lipid Panel-, Afinion HbA1c, and haemoglobin were written before data collection. All blood samples were analysed at the data collection site with Afinion 2 apparatus (Abbot diagnostics, US) , HemoCue Hb 201+ (Angelholm, Sweden) and Freestyle Freedom Lite glucometer (Abbot diagnostics, US), according to the SOPs.

Validation exercises to test the precision and reliability of Afinion Lipid Panel, Afinion HbA1c and HemoCue Hb 201+ were performed before data collection at Haukeland University Hospital. Results. The repeatability of the test was consistent, with low standard deviation, and low imprecision. The results are shown in appendix A3.

Two-level controls were performed on Lipid panel, and HbA1c weekly during data collection, and one-level control was performed on HemoCue four times a week. Between run standard deviation was low and the coefficient of variation was below 5% for all controls. Details are shown in appendix A4.

The same batch and lot number was used for all kits, respectively, to avoid lot specific analytical variations.

All the instruments were connected to a voltage stabilizer to avoid damage to instruments from the fluctuating voltage.

3.7 Data management

All questionnaires and biochemical results were recorded in paper forms during data collection at the site. All the data were manually double entered into a database using epidata entry client version 4.1.0.104. Validation steps were performed after data collection and after data entry. The data validation program was used on the two files, outliers and typing errors were corrected, and a new file created.

The data was exported to and analyzed using STATA V.16 (STATA corp, Texas, USA).

3.7.1 Data analysis

To create the diet diversity score of study participants, all food types were categorized into 11 different food groups using STATA. These 11 food groups included cereals, white tubers and roots, vegetables, fruits, meat, eggs, fish and other seafood, legumes, nuts and seeds, milk and milk products, oils and fats, and sweets. Using FAO guidelines for measuring individual diet diversity[44], nine final food groups were created, all starchy staples were categorized into one group, and all meat and fish-containing foods were categorized into one group. Individual diet diversity score (IDDS) was a score that was given to each individual and was based on the number of food groups that are consumed by the study population either daily, weekly, or monthly.

For the food frequency report, five frequencies were obtained from each participant: Daily, weekly, monthly, yearly, and never. Since there was a small difference between food reported consumed yearly and never, these variables were merged and called "rarely."

For the specific local dishes, the variable "daily and "weekly" were merged to create the variable ">1 a week". Information about macronutrients pr.100g for the specific local dishes was obtained from the Tanzanian food composition table[43].

Descriptive data are presented with median and ranges, and means and standard deviations (SD) or 95% confidence intervals for the continues variables. Frequencies and percentages are provided for the categorical variables. In the data analysis, factors that are associated with high HbA1c were assessed. A logistic regression model was applied using a threshold for high HbA1c set at 9.0%. The threshold for HbA1c was chosen because the value represents the population with poorly regulated diabetes. seA linear regression model was applied using duration of diabetes as the predictor variable. A bivariable assessment on socio-demographic, clinical, biochemical, and nutrition factors were done. Variables that showed significant associations with the outcome variable at the 0.05-level were included in the adjusted model. Crude (c) and adjusted (a) odds ratios (OR) and Coeff (β) were reported.

3.7.2 Handling of missing values

Body mass index was calculated using the standard formula (weight(kg)/height (m)*height (m)). Three participants were excluded from data capturing as they were paralyzed from the waist and unable to stand for weight measurements. We had not developed SOPs for anthropometric measurements for disabilities. The height for the disabled participants was measured using the length from the hip down to the leg, but measurements were excluded due to inaccurate data.

The fasting glucose assessment was supposed to be done at the clinic at the same time in the morning, but two participants measured fasting glucose at home before arrival to the study site. There were also two missing values for fasting glucose due to problems on the collection site. Similarly, there was one missing value for Haemoglobin measurements.

There were two missing for HDL and LDL results, due to Triglyceride being above 4mmol/L. There were two missing values for triglyceride and cholesterol values due to analytical instrument failure with troubleshooting code as an abnormal specimen. The samples were repeated, but the instrument reported the same error code. See Figure 5 for a detailed description of the number of data included in the descriptive data.

The clinical history information was based on self-report. Clinical verification of diabetes mellitus type 1, vision impairment, previous stroke, and numbness of lower limbs was not performed. One case report was missing; therefore, the total number of case report included in the descriptive tables is 59.

In the data analysis, no measures were taken to insert or replace any missing data, and the missing data was set to "missing."

3.8 Ethics

The study received ethical approval from the Norwegian Regional Ethical (REK) West Committee 5th of September 2019 with reference number 2019/766REK vest.
The study received approval from the Zanzibar Health Research Institute 21 October 2019, reference number; NO.ZAHREC/03/PR/Oct/2019/05. Data collection and recruitment was done at Mnazi Mmoja hospital in Zanzibar.

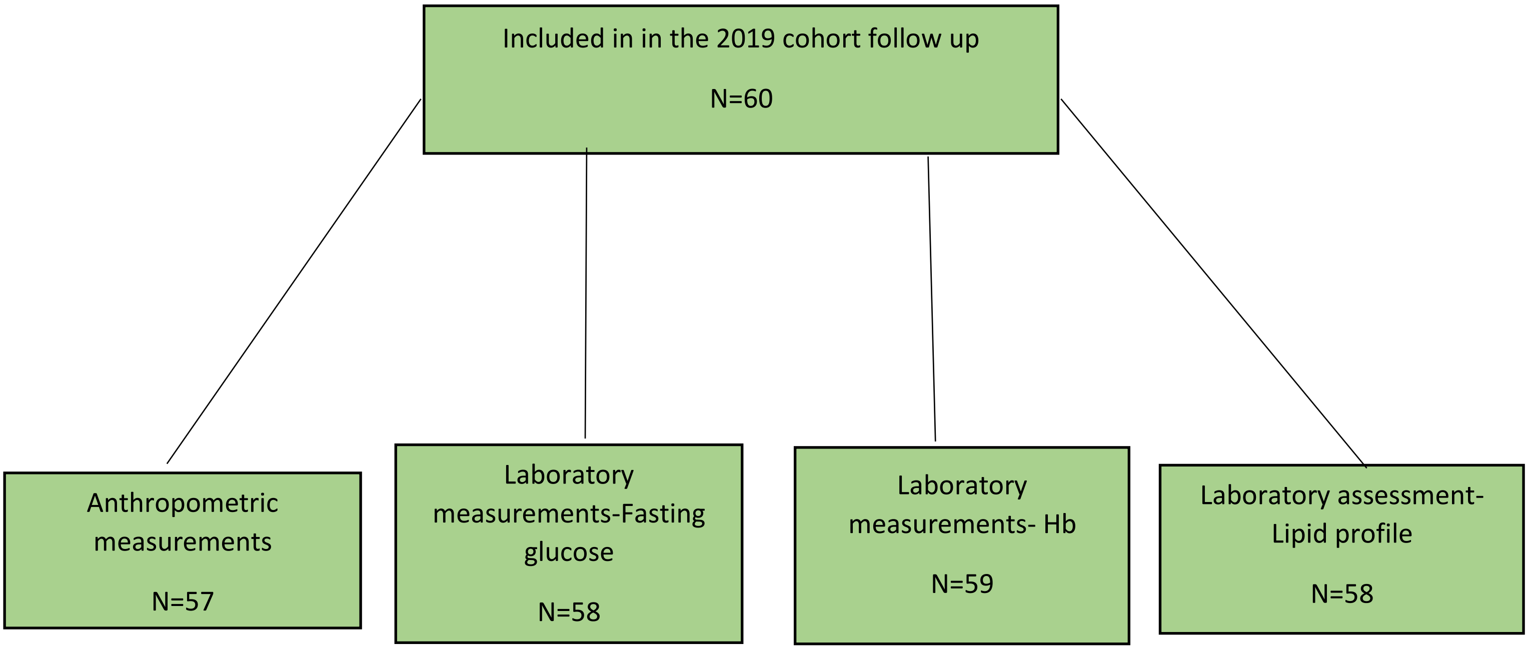

Figure 5, Overview of total number of patients results (n) included in the descriptive data and data analysis

4 RESULTS

4.1 Socio-economic characteristics of study population.

Sixty patients were included with a similar distribution of men and women. Table 1a and Table 1b, show continuous and categorical socio-demographic descriptive values of the study population. The majority of patients were above 50 years, with a mean age of 55 years. Out of the 32 that answered that they did not have income generating activities, 12 answered they received pension, 11 reported that others in the household worked and 9 reported different activities such as renting properties, fish trading and financial support from family members. The median years of schooling was 11, equivalent to form 4 in the Tanzanian school and educational system. Half of the participants had farming and cultivation activities. Participants reported that they cultivated a combination of vegetables and fruits that were used for household consumption, and the size of the plots that was used for cultivation purpose varied from two square meters to acres. All participants reported that the food budget consumed more than 90% of the total monthly income. More than 50% of the study population reported owning their houses and 40% reported living in urban areas of Zanzibar.

Table 2a Socio-economic characteristics of study population, continuous variables

Continues variables	Median, (min-max)
Age (years)	55 [32-80]
Education (Years)	11 [0-15]
Income (Thousand TZS)	350-400 [150 to >500)]
Food Budget (Thousand TZS)	350-400 [100 to >500)]

Table 1b Socio-economic characteristics of study population, categorical variables

Categorical variables	N(%)
Sex	
Male	33 (55%)
Female	27 (45%)
Region	
Urban	43 (71%)
Rural	15 (25%)
Income generating activities	
Yes	28 (47%)
No	32 (53%)
Farming and cultivation activities	
Yes	31 (52%)
No	29 (48%)
Ownership agricultural land	
Yes	16 (27%)
No	43 (73%)
Ownership house	
Yes	51 (85%)
No	9 (15%)

4.2 CLINICAL CHARACTERISTICS AND MEDICATION USE

Diabetes mellitus type 2 was the far most frequently reported condition reported, 47/60 (80%) of the participants. Only one participant reported to use diet regulation as treatment, the rest of the population was using either insulin treatment, oral antidiabetic treatment or a combination of both. Traditional medication was not frequently used among the study participants. Thirty percent of the study population was overweight (BMI 25.0-29.9kg/m2), and Obesity class 1 (BMI 30.0-34.9 kg/m2) was present in 24.6% of the population. When asked if participants had hypertension 47/60 (80%) answered “yes”. Blood pressure measurements at site showed that 38/60 (63%) had systolic blood pressure >140mmg/hg. Data on antihypertensive treatment was based on number of patients reported using one or more antihypertensive treatment and 55/60 (91.6%) reported using antihypertensive medications. Vision problems, numbness in limbs and pain in lower limbs were common reaching 56%, 67.8% and 45.8%, respectively. Participants were affected by ulcer either on toes or sole of feet, that was less common (18.4%), but 3/60 had amputations in lower limbs.

Table 2 Clinical diagnosis and medication use

Health indicator	N (%)
Type of diabetes	
DM type 1	7 (12.7%)
DM type 2	48 (87.2%)
Traditional medication	7 (12.3%)
Insulin treatment	35 (58.3%)
Oral antidiabetic treatment	37 (61.6%)
Antihypertensive treatment	55 (91.6%)
Lipid lowering therapy	4 (6.6%)
Anticoagulant medication	8 (13.3%)
Obesity	14 (24.5%)
Stroke	7 (11.8%)
Vision problems	33 (56%)
Numbness lower limbs	40 (67.8%)
Pain lower limbs	27 (45.8%)
Previous or current ulcer	11 (18.4%)
Amputation	3 (5.1%)

4.3 ANTHROPOMETRIC AND METABOLIC STATUS

The median and mean values for anthropometric and metabolic values (Table 3) were mostly similar indicating that the distribution curves were not too skewed, however, the exception was for F-Glucose where the median was lower than the mean. This indicates some left-skewing of that curve. Women tend to have lower haemoglobin level, 8 participants had haemoglobin levels below 11.5g/dl. However, women had higher mean systolic and diastolic blood pressure and were on average more overweight than men (>3kg/m2). The blood sugar levels were similar for men and women, both for F-Glucose and HbA1c. Mean value of LDL cholesterol was above optimal, and reaching to very high values for some participants. The mean value of total cholesterol was on the border line of the desirable level. However, 18/58 (31%) individuals had total cholesterol above 5.7, some of these patients were above 60 years of age. Only 4/60 (6.6%) participants reported using lipid lowering therapy, as seen in Table 2.

Table 3 Anthropometric and metabolic data of study population

Continues variables	Total median [min-max]	Total Mean±SD	Female Mean±SD	Male Mean ±SD
BMI	26.2 [18-42.4]	26.9±5.0	28.7±5.9	25.4±3.6
Systolic BP	140 [110-180]	141.2±16.0	145.5±14.5	137.6±16.4
Diastolic BP	90 [70-110]	89.9±8.6	91.5±7.6	88.6±9.3
F-Glucose (mmol/l)	10.8[3-27.8]	12.3±5.8	11.9±5.6	12.6±6.0
Hb (g/dl)	12.8 [8-15.5]	12.7±1.4	12.2±1.4	13.2±1.3
HbA1c (%)	9.1 [6-15]	9.5±2.1	9.8±2.2	9.4±2.1
HDL mmol/l	1.2 [0.46-2.59]	1.3±0.47		
LDL mmol/l	3.01 [0.5-5.7]	3.0±1.2		
Trig mmol/l	1.3[0.67-4.45]	1.6±0.8		
Total cholesterol mmol/l	5.0 [2.56-7.79]	5.1±1.3		

4.4 DIETARY PATTERNS

The results from the food frequency questionnaire are shown in Table 4 and Table 5, and presents 44 + 14 food types. Nearly all study participants reported alternation in the consumption frequency for staple foods, this means if the household consumed rice one day, the second day of the week cassava would be consumed, the third day potato would be consumed and by the fourth day plantain would be consumed. This was dependent on the monthly income, if the household had enough money, they would rather consume rice then cassava, sweet potato, potato and plantain. More than 80% of participants reported eating three meals a day and the portion sizes were usually larger for men compared to women. The remaining number reported eating two meals a day. White flour products are consumed on daily basis and could be consumed several times a day, manly as Buffalo, which is the local loaf of bread. The fruit consumption was frequent with more than half of the study population reported eating three different types of fruit on a weekly basis. Some of the food types that were rarely eaten, include foods that were consumed only during special religious occasions, such as Christmas and Ramadhan. These food types might be consumed weekly or daily during these holidays. This included foods such as dates and pasta. Protein rich food groups such as small sardines and kidney beans was consumed regularly in a soup made with tomato and occra.

14 local Zanzibarian dishes were also included in the food frequency report (Figure 5). These dishes are prepared either using a substantial amount of oil or is deep fried and are made using white flour. These food types are therefore high in saturated fatty acids (SATFAT) and have a high glycaemic load. Two dishes, Katlesi and Uroju soup, were not found in the *Tanzanian food composition table* and therefore information on macronutrients was not found. Eight out of the fourteen food types were consumed more than once a week and therefore relatively frequently by most of the study participants. There are two types of oil that were used by participants, palm oil and sunflower oil were used by 23.2%, and 71.4% of the participants, respectively. A combination of both palm oil and sunflower oil was used by 3% of the participants. Furthermore 58% of the study participants used coconut milk either as a substitute for oil or in combination with oil more than once a week. All participants used homemade coconut milk.

Table 4 Semiquantitative general food frequency questionnaire results. The table includes the specific foods groups and each column has a frequency that is highlighted, and this represents the frequency of the food type that the highest number of participants reported.

Total (n)	Types of food	Daily	Weekly	Monthly	Rarerly	Average portion size
(n=60)	Sweet Banana	5 (8%)	33 (55%)	11 (18%)	11 (18%)	1 small banana
(n=60)	Orange raw	5 (8%)	27 (45%)	14 (23%)	14 (23%)	1 Orange
(n=60)	Mandarin raw	0 (0%)	1 (2%)	1 (2%)	58 (97%)	1 Mandarin
(n=60)	Mango raw	8 (13%)	36 (60%)	6 (10%)	10 (17%)	1 Mango
(n=60)	Dates raw	1 (2%)	10 (17%)	18 (30%)	31 (52%)	4-7 dates
(n=60)	Apples raw	2 (3%)	14 (23%)	14 (23%)	30 (50%)	
(n=60)	Coconut milk	4 (7%)	35 (58%)	8 (13%)	13 (22%)	Small bowl
(n=60)	Coconut water	0 (0%)	12 (20%)	25 (42%)	23 (38%)	1 coconut
(n=60)	Papaya raw	2 (3%)	32 (53%)	15 (25%)	11 (18%)	1/4 slice
(n=59)	Passionfruit raw	0 (0%)	14 (24%)	13 (22%)	32 (54%)	1 passionfruit
(n=60)	Homemade juice	4 (7%)	20 (33%)	19 (32%)	17 (28%)	1 glass
(n=60)	Store bought juice	0%	0%	5 (8%)	55 (92%)	1/2 glass
(n=60)	Plantain	2 (3%)	35 (58%)	19 (32%)	4 (7%)	Medium sized plate
	Avocado	0%	10 (18%)	12 (21%)	34 (60%)	1/2 avokado
(n=60)	Morringa leaves	0%	3 (5%)	1 (2%)	56 (93%)	Small sized plate
(n=60)	Spinach	4 (7%)	46 (77)%	7 (12%)	3 (5%)	Small sized plate

(n=60)	Tomato	41 (68%)	18 (30%)	0%	1 (2%)	3-5 tomatoes
(n=60)	Occra	21 (35%)	30 (50%)	2 (3%)	7 (12%)	2-3 Occra
(n=60)	Cassava leaf	0%	17 (28%)	28 (47%)	15 (25%)	Small bowl
(n=60)	Cassava	0%	14 (23%)	34 (57%)	12 (20%)	Medium sized plate
(n=60)	Sweet potato	0%	9 (15%)	19 (32%)	32 (53%)	Medium sized plate
(n=59)	Potato	15 (25%)	20 (34%)	8 (14%)	16 (27%)	1-2 potatoes
(n=60)	Oil	14 (23%)	40 (67%)	4 (7%)	2(3%)	Small bowl
(n=60)	White flour	27 (45%)	28(47%)	3 (5%)	2(3%)	-
(n=60)	Rice	11 (18%)	43 (72%)	6 (10%)	0 (0%)	Medium sized plate
(n=58)	Maize (raw)	0%	11 (19%)	12 (21%)	35 (60%)	1 colbe
(n=56)	Porridge	10 (18%)	8 (14%)	6 (11%)	32 (57%)	Medium sized bowl
(n=60)	Pasta	0%	4 (7%)	7 (12%)	49 (82%)	small plate
(n=60)	Kidney beans	0%	46 (77%)	9 (15%)	5 (8%)	Medium sized bowl
(n=60)	Chickpeas	1 (2%)	13 (22%)	9 (15%)	37 (62%)	Small bowl
(n=60)	Peanuts	6 (10%)	27 (45%)	17 (28%)	10 (17%)	200 g pack
(n=60)	Cashew	0%	4 (7%)	16 (27%)	40 (67%)	small handfull
(n=59)	Red meat	0%	25 (42%)	24 (41%)	10 (17%)	1-3 pieces
(n=60)	Processed meat	0%	1 (2%)	0%	59 (98%)	
(n=60)	Chicken	1 (2%)	28 (47%)	21 (35%)	10 (17%)	One drumstick
(n=60)	Egg	2 (3%)	32 (53%)	15 (25%)	11 (18%)	1-2 eggs
(n=60)	Fish	9 (15%)	30 (50%)	13 (22%)	8 (13%)	1/2 slice-1 slice

(n=60)	dagaa (sardines)	21(35%)	30 (50%)	3 (5%)	6 (10%)	small bowl
(n=60)	Milk	7 (12%)	28 (47%)	10 (17%)	15 (25%)	One cup
(n=59)	Yoghurt	0%	5 (8%)	4 (7)%	50 (85%)	half of the small bowl
(n=59)	Butter	2 (3%)	8 (14%)	3 (5%)	46 (78%)	Tea spoon
(n=58)	Buffalo	25 (43%)	24 (41%)	1 (2%)	8 (14%)	One buffalo (630g)
(n=55)	Soda	0%	3 (5%)	5 (9%)	47 (85%)	One cup

Table 5 Semiquantitative food frequency report of specific local dishes

			Consumption frequency				Macronutrient	
Total (n)	***Local dishes***	***Recipe describtion***	***>1 a week***	***Monthly***	***Rarerly***	***Portion Size[3]***	***SATFAT[1]***	***Energy[2]***
n=57	Maandazi	African donut	44% (25)	18% (10)	37% (22)	58-116g	8.7	359.7
n=55	Mkate ufuta	Bread made with coconut milk	18% (10)	35% (19)	47% (26)	150g	0.6	274
n=60	Mkate wa Mchele	Bread made with rice	8% (5)	12% (7)	80% (48)	150g	6.3	239.1
n=60	Badia	Deep fried chickpeas	37% (22)	25% (15)	38% (23)	200g	0.68	356
n=60	Katlesi	Deep fried potato and fish cutlet	20% (12)	32% (19)	48% (29)	1 pr portion		
n=60	Pilau	Rice w/local spices	52% (31)	28% (17)	20% (12)	250 g	3.1	177
n=60	Biriyani	Rice w/tomato sauce and beef	2% (1)	12% (7)	87% (52)	250 g	5.3	208
n=60	Chapati	Bread made with ghee	52% (31)	27% (16)	22% (13)	144 g	16.5	372.6

n=60	Sambusa	Deep fried pastry with different filling	8% (5)	15% (9)	77% (46)	100 g	3.5	280
n=60	Chipsi mayai	Deep fried potato with fried egg	10% (6)	18% (11)	72% (43)	150 g	15.3	246
n=60	Fried cassava chips		32% (19)	28% (17)	40% (24)	Small sized pack	0.2	288
n=60	Urojo soup	Soup with fried potato, grilled beef and egg	38% (23)	23% (14)	38% (23)	350 g		
n=60	Mshikaki	Grilled meat	36% (21)	16% (9)	48% (28)	2 sticks	10.6	343
n=59	Halawa	Sweets made with flour, cococnut milk and ghee	0% (0)	12% (8)	88% (52)	15 g	16.9	511.7

[1] Saturated fatty acid pr. 100g. [2] Energy in Kcal pr. 100g. [3] Average portion size reported from participants

4.5 INDIVIDUAL DIET DIVERSITY SCORES

The minimum diet diversity score observed was 4 and the maximum diet diversity score was 9 (Table 7). It was most common to have IDDS of 8, representing eight food groups (Table 6). The food groups were aggregated according to WHO guidelines for making individual diet diversity scores, and the is presented in Table 7.

Table 6 Individual diet diversity score of study population

IDDS[1]	Total (n=52)	Percentage	
4	1	1.92	
5	1	1.92	
6	4	7.69	
7	15	28.85	
8	20	38.46	
9	11	21.15	
Total	**52**	**100**	

[1] *Individual diet diversity score*

Table 7, Mean and Median values of the individual diet diversity score

Mean ± SD	Median (Min-Max)
7.6 ± 0.15	8 (4-9)

Table 8 Aggregation of food groups from the Food Frequency Questionnaire to create Individual dietary diversity score . According to the WHOs guidelines for measuring household and individual diet diversity, food group 1 (Starchy staples) is a combination of the two food groups cereals and white tubers. Food group 4 (Meat and Fish) is a combination of meat products and fish products.

Food Group 1	Food Group 2	Food Group 3	Food Group 4	Food Group 5	Food Group 6	Food Group 7	Food Group 8	Food Group 9
Starchy staples	Vegetables	Fruits	Meat and fish	Egg	Legumes and Nuts	Diary products	Oils and Fats	Sugar and sweets
Cereals	Occra	Banana	**Meat products**	Egg	Kidney beans	Milk	Butter	Halawa
Rice	Tomato	Orange	Mshikaki		Chickpeas	Youghurt	Oil	Soda
Ugali	Spinach	Mango	Red meat		Peanuts		Coconut milk	
Uji	Morringa leaves	Apple	Chicken		Cashew nuts			
Sembe	Cassava Leaves	Coconut water	**Fish products**					
White flour	Corn	Papaya	Sardines					
Pasta		Passionfruit	Other fish					
White Tubers		Homemade Juice						
Plantain		Dates						
Cassava		Avokado						
Sweet potato								
Regular potato								

4.6 ASSOCIATION BETWEEN METABOLIC STATUS, DIETARY PATTERNS, SOCIO-ECONOMY, AND NEUROMUSCULAR SYMPTOMS

HbA1c levels were dichotomised at 9.0%. Values that are above 9.0% were considered as poorly regulated diabetes and HbA1c levels below 9.0% were considered as moderate and better regulated diabetes. The 0- hypothesis was that there is no association between HbA1c ≥ 9.0% and socio-demographic, health and dietary factors.

The regression analysis showed no significant difference between males and female and having poorly regulated diabetes. There was a significant association between HbA1c levels ≥9.0% and age, unemployment and not having cultivation activities. There is not enough statistical evidence that HbA1c levels above 9.0% has a positive association with any of the neuromuscular symptoms such as ulcer, reduced vision, and numbness lower limbs of this study population. Age and unemployment have the same odds ratio, protective exposure, in the adjusted model as in the crude model, but only unemployment was statistically significant. The regression analysis also shows that the confidence interval of the estimate was broad for almost all of the outcome variables, and there are small differences in the odds ratio as evident by the number of cases for each of the predictor variables. Interpretation of these estimates should therefore be done with care, even though the p-value is significant for some outcomes.

Table 9, overview of a crude regression and adjusted analysis with HbA1c as the response variable.

HbA1c	HbA1C≤9.0	HbA1C≥9.0						
	N=27	N=33						
Predictor variables	*N (%)*	*N (%)*	*C OR*	*[95% CI]*	*P-value*	*A OR*	*[95% CI]*	*P-value*
Sex (Female)	11 (40.7%)	16 (48.5%)	1.4	[0.5-3.8]	0.55	0.5	[0.1-1.7]	0.27
Age, ≥ 50 years	21 (77.8%)	17 (51.5%)	0.3	[0.09-0.94]	0.04	0.5	[0.1-1.8]	0.29
BMI≥30	6 (24%)	8 (25%)	1.1	[0.3-3.6]	0.93			
Systolic BP≥140mmHg	17 (62.9%)	21 (63.6%)	1.0	[0.3-3.0]	0.96			
Numbness lower limbs	17 (65.4%)	23 (69.7%)	0.8	[0.3-2.5]	0.73			
Ulcer*	5 (19.2%)	6 (18.2%)	1.1	[0.3-4.0]	0.92			

Reduced vision	16 (61.5%)	17 (51.5%)	1.5	[0.5-4.3]	0.44			
Insulin treatment*	13 (48.2%)	20 (60.6%)	0.5	[0.2-1.2]	0.11			
Unemployment	19 (59.4%)	13 (39.4%)	0.3	[0.09-0.8]	0.02	0.3	[0.07-1.0]	0.055
No cultivation activities	9 (33.3%)	20 (60.6%	3.1	[1.06-9.0]	0.04	2.9	[0.9-9.0]	0.07
Diet diversity score ≥8	14 (60.9%	17 (58.6%)	0.9	[0.3-2.7]	0.87			
Portion size of rice (Large)	7 (26.9%)	5 (16.1%)	0.6	[0.1-2.5]	0.46			
Daily consumption of local loaf bread	8 (29.6%)	17 (54.8%)	2.9	[1.0-8.6]	0.056			

4.6.1 Association between duration of diabetes, health and nutrition.

A linear regression model was used to understand the effect of long-term diabetes and how it is associated with the neuromuscular complications, nutrition and socio-economy. In the bivariable analysis a significant association was observed between developing ulcers and the duration of diabetes. This was not observed for complications such as reduced vision and numbness lower limbs. There is also statistical evidence that there is an association between the duration of diabetes and insulin treatment. In the adjusted model, only age was significant and a weak significance was observed for increasing diet diversity score and duration of diabetes. The Odds ratio is close to one for all outcome variables, except foot ulcer which shows that the duration of diabetes has a effect on ulcer even in the adjusted model. The same wide confidence interval is seen in the linear regression as in the logistic regression, indicating interpretation with care.

Table 10 linear regression analysis of duration of diabetes, health and lifestyle.

Duration of diabetes	β	[95% CI]	P-value	β adjusted	[95% CI]	P-value
Predictor variables						
Sex	-0.8	[-4.7 to 3.1]	0.68			

Age, Years	-0.2	[-0.4 to -0.02]	0.03	-0.2	[-0.4 to -0.04]	0.015
BMI ≥30.0	1.9	[-2.7 to 6.5]	0.41			
Systolic BP ≥140mm/hg	-3.7	[-7.6 to 0.3]	0.07			
Foot-Ulcer	5.7	[0.8-10.6]	0.02	3.7	[-1.2 to 8.6]	0.13
Numbness lower limbs	2.7	[-1.4 to 6.7]	0.19			
Reduces Vision	1.7	[-2.1 to 5.6]	0.37			
Insulin treatment	2.6	[0.69 to 4.5]	0.01	2.0	[-0.3 to 4.3]	0.09
Unemployment	-0.7	[-4.5 to 3.2]	0.73			
No cultivation activities	3.4	[-0.4 to 7.1]	0.079			
Diet Diversity Score	1.8	[-0.03 to 3.7]	0.054	1.7	[0.2 to 3.5]	0.048
Portion size of rice	0.3	[-2.4 to 3.0]	0.85			
Consumption frequency of the local loaf bread	0.4	[-1.1 to 1.9]	0.58			

5 DISCUSSION

To our knowledge this is the first clinical cohort with dietary assessment that has been conducted on diabetes patients in Zanzibar. The cohort has provided interesting data about diet habits and metabolic status. Below follows a discussion of findings and methods.

The aim of this study was to investigate the nutritional and health related factors of diabetic patients in Zanzibar. The factors include socio-economic, dietary, anthropometric, biochemical, and clinical aspects.

5.1 DISCUSSION OF FINDINGS

The baseline study in 2014 included 100 diabetic patients[45]. This follow up included 62% of the originally included patients. The cause of death of the 14% are not medically verified, but family members confirmed cases like ketoacidosis, cardiovascular arrest and cerebrocardiovascular accidents (CVA). The records from the Mnazi Mmoja medical ward and intensive care unit (ICU), show that the leading cause of admission from 2016-2018 was cardiovascular arrest and CVA, which substantiates that this is a possibility.

The findings from the socio-economic characteristics show that the income level is on the average level compared to the population of Zanzibar, most of the study participants where residing in the urban areas, where there is more work opportunities in the both private and governmental sector. It should be mentioned that the income level could be biased, as culturally it is not common to ask about income in Zanzibar and some study participants were hesitant when asked this question.

Half of the population reported not having income generating activities, however 12 participants reported that others in the household work, and 11 reported receiving pensions. It is less common for women to work in Zanzibar and since 45% of the included participants were female this could explain the high unemployment rate. Women also had higher mean BMI than men, this could be to female physiology, but it could also be due to inactivity.

Economically Unguja relies heavily on the tourism sector. Investments in this sector have increased the demand of land. As many farmers are poor it is difficult to resist offers received from the investment companies. This practise brings down the agricultural activities of the Island, and the outcome can be increasing food prices. Findings from this study showed that the estimated food budget for the study population, exceeded income level with >90%. This is supported by another food habit study conducted in Zanzibar [46], that studied how fruit and vegetables consumption effect systolic and diastolic blood pressure, among the findings was a high food budget for households. Reduced food accessibility can force patients to make unhealthy nutrition choices.

The mean HbA1c in our study population was 9.5%, suggesting poorly regulated diabetes mellitus. The population was not anaemic as the mean Hb level was 11.9g/dl for women and 12.6 g/dl for men. This indicates that the HbA1c levels are not falsely lower or higher than the mean value due to hemoglobinopathies. The systolic and diastolic blood pressure were both on the limit of the hypertension cut-off (140/90 mm/hg). The mean fasting glucose measurements were 12.3mmol/L, which supports the HbA1c findings. Only 11 individuals had a HbA1c below 7.5%, which is the recommended level to avoid serious health complications related to diabetes.

Although both genetic and environmental factors contribute to the metabolic state in these patients[47], an important influenceable factor is the diet and the use of medication accordingly. The diet assessments showed that food groups high in glycaemic load such as sweet banana, bread, rice, potato, plantain and fried local dishes are consumed more than once a week. The local buffalo bread is consumed daily and could be consumed several times a day by 43% of the study population, it is important to notice that one load of bread is about 630g.

The most common diet diversity score was between seven and eight. The utilization of food seems to be adequate as evident by the individual diet diversity score, however the mean score might be lower if we were to exclude food groups that are consumed monthly from the analysis. The finding suggest that these patients are not severe food insecure, but rather the availability and utilization of food that are low in glycaemic load (GL) is poor. Crops such as sweet potato and protein rich products such as eggs, is eaten significantly less frequent than high GL foods, such as bread, rice and chicken. Many study participants were under the impression that sweet potato was not good for diabetic patients, and that rice consumption was a healthier choice.

When asked if participants had hypertension 47/60 (80%) answered “yes”. Blood pressure measurements at site showed that 38/60 (63%) had systolic blood pressure >140mmg/hg. Data on antihypertensive treatment was based on number of patients reported using one or more antihypertensive treatment and 55/60 (91.6%) reported using antihypertensive medications. These findings might indicate that there is under diagnostical issues and communication barrier between the health sector and the patients. It is unclear if the 10% that answered they did not have hypertension, but were still taken medication, misunderstood what was asked or if they need to be better informed about their diagnosis. Considering that 63% of the population had high blood pressure readings at site, the patients might not respond accordingly to the medication dosage prescribed.

The mean value of total cholesterol was on the border line of desirable level. However, 18/58 (31%) individuals had total cholesterol above 5.7, some of these patients were above 60 years of age. Only 4/60 (6.6%) participants reported using lipid lowering therapy. Consistent with the baseline study, there is still a large gap in lipid lowering therapy. This could be due to the fact that only the private laboratories provide lipid profile analysis, and therefore not economically available for the most people.

5.1.1 Discussion of the linear regression and the logistic analysis

The crude and adjusted logistic analysis showed wide confidence intervals for all of the estimates and the odds ratio was close to one. Daily consumption of the local loaf bread seems to have an effect on the HbA1c levels, but the effect size is impossible to interpret because of the wide confidence interval. The analysis also shows that females seem to be more exposed to HbA1c above 9.0%. Another interesting finding is the protective effect unemployment seem to have on the HbA1c levels, which could be explained by the fact that employment results in better economic position and therefore a different diet behaviour. It is important to underline that due to the small sample size, the estimates do not reflect the population with high certainty. Therefore the interpretation of this analysis is difficult, and should be done with care.

The logistic model also shows protective odds ratio for patients ≥ 50 years, suggesting that the elderly might have better glycaemic control in this cohort and might have better diabetes care. These findings are interesting, and should be interpreted with care. However, a meta-study conducted on the availability of diabetes care in 12 countries in Sub-Saharan Africa in 2016[10] found that the need for diabetes care was significantly more likely to be met in the older diabetes patients. Four to seven measures were met for older patients, among these was counselling on nutrition, exercise, use of oral anti diabetic medication and insulin treatment. The measures mentioned in the (Manne-Goehler, J., et al, 2016) could be translated to our study population due to several factors (1) younger patients might avoid attending to the clinic in Mnazi Mmoja due to stigmatization, (2) there is a great strong sense of care and respect for the elderly in the culture (3) elderly are financially more strong because in Zanzibar they live in large households and are rarely left to live alone. Another possible explanation is that older patients eat less due to loss of appetite.

Several studies has shown that a increase in HbA1c and glucose levels also results increase in retinopathy in long term diabetic patients. However, this was not evident in our logistic regression analysis as we saw no significant association with reported impaired vision and poorly regulated diabetes *(p-0.44, [CI 0.5-4.3]).* This could be due to the fact that the data from our study population is self reported and not clinically verified, this means that our study participants may have answered that they have troubles with eyesight due to being far sighted or near sighted and not reduced vision. It could also be that our sample size is not large enough to detect an association.

In our linear regression analysis a significant positive association was seen between reported ulcer and year of diabetes diagnosis *(p-0.02, [CI 0.8-10.6])* and not between numbness lower limbs and diabetes diagnosis *(p-0.19, [CI -1.4 to 6.7]).* Numbness lower limbs is sensational and is a complication that is not seen optical, this could make it hard to distinguish between a progressive neuromuscular damage or just pain due to other external factors. Ulcer can be seen physically and has to be medically treated, so the probability of reporting that a patient has a wound could be higher than reporting on a sensation.

The diet diversity score is borderline significant in the linear regression model. The increased DDS may be associated with diabetes duration due to patients receiving more education on the importance of diversification.

The metabolic profile and complication rate in this cohort has not improved since baseline in 2015 and the mortality rate was high (14%). This understates the need for improved diabetes care in Zanzibar.

5.2 Discussion of methods

A important limitation of the study is that all complication cases where self reported and not clinically verified, due to lack of resources at study site. It was not possible to test the agreement between the self-reported cases and medical records. There is no electronic filing system in Mnazi Mmoja and manual filed records that are more than 10 years are impossible to find in Mnazi Mmoja Hospital.

Another limitation was the follow up procedure, and the sample size of the study. The diabetic clinic do not keep telephone records of patients and have a manual register of the patients. Therefore 40% of the participants where impossible to reach due to changes in registered phone numbers from the baseline study. The hospital only registers death within the hospital, therefore the 14% that were deceased were not confirmed medically. Neither, were there research resources to maintain the contact details between the assessments.

The Tanzanian food composition table is a scientific tool that was used to understand usual portion sized in Tanzania, but Zanzibar is different in some of the food culture compared to Tanzania. Scientific supplementation of the existing data on food types and nutrients proved to be difficult as there is no data available for the Island of Zanzibar. Therefore the Tanzanian composition table partially covered food items and nutrient content used in Zanzibar.
A thorough training on how to conduct dietary assessment in a low resource setting, should

also have been conducted both on the study nurse, study doctor and the master student, weeks before data collection.

5.2.1 Limitation of food frequency recall

The FFQ should have been validated before it was used in this study. Validation includes pre-testing a small population that is within the study setting to understand the strength and weaknesses of the FFQ [34]. To acquire accurate portion sizes food groups that were used in the FFQ , food types should have been weighed and standardized, before categorizing them into the used terms in the final FFQ. We conducted a small marked research to the estimated sizes in grams of some food items, such as cassava chips, cashew, buffalo bread, peanuts and halawa. Using a FFQ includes both systematic and random errors [48]. These errors might be person specific or intake-related. Intake related bias is seen when the actual intake is not correlated with the reported intake, and could for example be driven by socio-economic pressure to answer accordingly. For this study setting, overreporting eating habits in order to be seen as economically stable, and underreporting to be perceived as a healthy individual is a possibility. Person specific bias is when the reported intake is unusual if the FFQ would have been reported on a different day [48]. In this study patients might have recalled a different frequency of eating habits if asked again during a economically unstable year or month.

5.2.2 Limitation of analytical instruments

Venous blood collection for fasting plasma glucose is considered to be the gold standard, however WHO accepts the use of capillary glucose apparatus in low income settings. Capillary blood sugar tends to be 10% lower than fasting plasma glucose.

The apparatus that were used were all point of care instruments and have limited test range, temperature and light sensitive and might compensate to a less extent for intra induvial analytical variations, such as drug use, and pathological disorders.

5.3 Conclusion

The nutritional and health factors investigated suggest a population with poor diabetes management as evident by the metabolic and diet assessments. Diet is high in refined carbohydrates. with a high diet diversity score. There is no improvement in HbA1c or blood pressure since control since the start in 2015 and the number of complications have not decreased. Undermedication of both lipid lowering therapy and antihypertensive therapy is till represented in the study population.

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APPENDIX

Table A1, FFQ general food groups

Food frequency questionnaire

Standards question: How often do you eat ....?

What is the serving size of the item you eat?

How often do you eat this

Was this consumed yesterday?

All of the question below are based on food you consume this season.

Starting question:

How many meals do you eat in one day?

Food/drinks	Comments	Serving size			Was this food consumed yesterday?		How often is this consumed?				
		S	M	L	Yes	No	D	W	M	Y	N
Sweet Banana (cooked, **fried** or boiled?)											
Orange (raw)											
Mandarin (raw)											
Mango (raw)											
Dates											
Apples (raw)											
Coconut milk (homemade or **store bought**?											
Coconut water/madafu											
Papaya (raw)											
Passionfruit (raw)											
Homemade juice (Specify)											
Store bought juice (Specify))											
Cooking banana/Plantain											
Mhlonge (moringa)											
Spinach (Cooked, Fried or raw?)											
Tomato (Cooked, Fried or raw?)											
Auccra											
Cassava leaf											
Yams (cooked, fried or boiled?)											
Yam leafs											
Cassava (cooked or fried?)											
Sweet potato (Cooked, Fried?)											
Potato (Cooked, Fried?)											
Oil (**what type**?)											
White flour											
Rice (**What type**?)											
Maize (flour or raw?)											
Pasta											
Kidney beans (fried or cooked?											
Chickpeas											
Peanuts											
Cashew											
Red meat											
Processed meat											
Chicken											
Egg											
Fish (including the small ones)											
Milk (full fat or low fat?)											
Yoghurt											
Butter											

Table A2, Continue of the FFQ, specific local dishes.

	I am now going to list food types that is common in Zanzibar. Please tell me how often you eat these food types and how big your portion normally is.										
Maandazi											
Mkate wa Mchele (kumimina)											
Badia											
Katlesi											
Pilau											
Biriyani											
Ndizi-nyama											
Ugali											
Chapati											
Sambusa											
Bamia											
Maharage											
Chipsi mayai											
Fried cassava chips											
Urojo soup											
Pweza wa nazi											
Mshikaki											
Halawa											

Tabel A3 represents precision test preformed on Affinion 2 and Hemocue Hb 201+.

	Repterbarhet Afinion 2. (1 prøve pr analytt, 20 ganger)					Hemocue Hb 201+
Dato	Prøvenummer	HbA1c. **mmol/mol**	Prøvenummer	Kolesterol. **mmol/l**	Prøvenummer	Hemoglobin. **g/dl**
11/10/2019	81934360	72	31520960	8.77	31527625	11.90
11/10/2019	81934360	70	31520960	9.56	31527625	12.00
11/10/2019	81934360	68	31520960	9.11	31527625	11.90
11/10/2019	81934360	71	31520960	9.06	31527625	11.90
11/10/2019	81934360	68	31520960	9.21	31527625	12.10
11/10/2019	81934360	68	31520960	8.81	31527625	12.00
11/10/2019	81934360	68	31520960	9.53	31527625	12.00
11/10/2019	81934360	68	31520960	8.63	31527625	12.00
11/10/2019	81934360	69	31520960	9.68	31527625	11.60
11/10/2019	81934360	67	31520960	8.84	31527625	12.00
11/10/2019	81934360	69	31520960	9.33	31527625	12.00
11/10/2019	81934360	67	31520960	9.39	31527625	11.90
11/10/2019	81934360	68	31520960	8.87	31527625	12.10
11/10/2019	81934360	68	31520960	8.63	31527625	11.90
11/10/2019	81934360	69	31520960	8.88	31527625	12.00
11/10/2019	81934360	67	31520960	9.09	31527625	12.10
11/10/2019	81934360	67	31520960	8.91	31527625	12.10
11/10/2019	81934360	68	31520960	8.78	31527625	12.00
11/10/2019	81934360	68	31520960	8.8	31527625	11.90
11/10/2019	81934360	67	31520960		31527625	12.10
	Gjennomsnitt	68.35		9.05		11.98
	Standardavvik	1.31		0.31		0.11
	CV	1.92		3.46		0.92

God riktighet, sammenlignet med svar fra medisinsk biokjemi

	Riktighet/ prøvesvar fra MBF	
HbA1c	mmol/mol. Ref. lab	mmol/mol. Afinion 2
70479288	49.00	50.00
81934360	67.00	72.00
31526142	33.00	34.00
Hb		
31527625	12.20	11.90
31527726	16.60	16.80
31527116	7.70	7.60
Kolesterol	*Serum*	*EDTA*
31514913	2.19	2.67
70452305	4.00	4.68
31520960	8.96	9.12

		Reagens informasjon	
	HbA1c	lipid panel	hemoglobin
lot	10203124	10204225	1908477
utløps	11/06/2021	01/09/2020	12/08/2020

		QC informasjon	
		HbA1c	
			Range kontroll
C1 Lot	10202640	41 mmol/l	
C2 lot	10202594	65mmol/l	
Utløpsdato			
		Kolesterol	
			Range kontroll
C1 Lot	10201763	4,23mmol/l	
C2 Lot	10201704	231mg/dl	
Utløpsdato			
		Hemoglobin	
Lot	92102		Range kontroll
Utløpsdato	2020/12	11,7 g/dl	12,0 ± 0,6 g/dl

Tabel A4

Result of level I and level II controls, between run standard deviation and calculated coefficient of variation for HbA1c, lipid panel and haemoglobin controls.

		HbA1c kontroll	Lipid Panel kontrol					Hemoglobin Kontroll					
Date	Level of control	HbA1c (%)	Kolesterol (mmol/l)	LDL (mmol/l)	HDL (mmol/l)	Triglycerider (mmol/L)	kommentarer		Dato	Hb (g/dl)			
									11.10.19	11.7	Første kontroll		
11.10.19	Level II	8.1	5.97	3.10	1.60	2.77			28.10.19	11.6	Første kontroll		
28.10.19	Level II	8.1	5.93	3.12	1.56	2.74			04.11.19		Første kontroll	IKKE KJØRT	
04.11.19	Level II	8.0	6.14	3.31	1.58	2.74			01.11.19	11.6	Første kontroll		
06.11.19	Level II	8.0	6.46	3.51	1.62	2.92			04.11.19	11.6	Første kontroll		
11.11.19	level II	8.0	6.32	3.40	1.60	2.90			06.11.19	11.6	Første kontroll		
15.11.19	Level II	8.1					Pga. Ustabil strøm		08.11.19	11.7	Første kontroll		
18.11.19	Level II	8.0						Normal level	11.11.19	11.6	Første kontroll		
19.11.19	Level II		6.37	3.48	1.61	2.81	Ingen pasienter. Kjørt pga. ustabil strøm		12.11.19	11.5	Ny kontroll		
25.11.19	Level II	8.0	6.22	3.31	1.62	2.83			13.11.19	11.6	Første kontroll		
03.12.19	Level II	8.0	6.20	3.35	1.57	2.82			14.11.19	11.7	Første kontroll		
17.12.19	Level II	8.0							15.11.19	11.6			
Date	Level of control	HbA1c (%)	Kolesterol (mmol/l)	LDL (mmol/l)	HDL (mmol/l)	Triglycerider (mmol/L)			19.11.19	11.6		18.11.19	ingen pasienter
11.10.19	Level I	6.0	4.32	2.56	1.08	1.49			20.11.19	11.6			
28.10.19	Level I	6.2	4.41	2.72	1.03	1.45			21.11.19	11.9			
04.11.19	level I	5.8	4.71	2.93	1.08	1.55			25.11.19	11.6	Ny kontroll	Åpnet 12.11.19	
06.11.19	Level I	5.9	4.73	2.9	1.11	1.58			26.11.19	11.5			
11.11.19	Level I	5.9	4.68	2.92	1.06	1.55			27.11.19	11.7			
18.11.19	Level I	5.9					Pga. Ustabil strøm		28.11.19	11.5			
19.11.19	Level I		4.82	3	1.1	1.59	Ingen pasienter. Kjørt pga. ustabil strøm		03.12.19	11.7			
25.11.19	Level I	5.9	4.57	2.81	1.07	1.52			04.12.19	11.7			
03.12.19	Level I	5.9	4.70	2.93	1.10	1.60							
17.12.19	Level I	5.9											

	Middelverdi	
Level I HbA1c (%)	5.9	
Level II HbA1c (%)	8.03	
	SD	
Level I HbA1c (%)	0.046	
Level II HbA1c (%)	0.105	
	CV	
	0.77	%CV LEVEL I
	1.31	%CV LEVEL II

	Middelverdi	
Level I Total.chol	4.6	
Level II Total.chol	6.2	
	SD	
Level I Total.chol	0.16	
Level II Total.chol	0.17	
	CV	
	3.5	%CV LEVEL I
	2.8	%CV LEVEL II

	Middelverdi	
Level I HDL chol	1.08	
Level II HDL chol	1.60	
	SD	
Level I HDL chol	0.024	
Level II HDL chol	0.021	
	CV	
	2.2	%CV LEVEL I
	1.3	%CV LEVEL II

	Middelverdi	
Level I LDL chol	2.8	
Level II LDL chol	3.3	
	SD	
Level I LDL chol	0.13	
Level II LDL chol	0.14	
	CV	
	4.7	%CV LEVEL I
	4.2	%CV LEVEL II

	Middelverdi	
Level I Trig	1.5	
Level II Trig	2.8	
	SD	
Level I Trig	0.049	
Level II Trig	0.063	
	CV	
	3.2	%CV LEVEL I
	2.3	%CV LEVEL II

Hemocue normal level presisjon	
Middelverdi	
11.63	
SD	
0.09	
CV	
0.77	%CV Normal level