The Islamic University–Gaza
Research and Postgraduate Affairs
Faculty of science
Master of Biological Sciences
Medical Technology

الجامعـــــــة الإســـلاميـة – غـزة
شئون البحث العلمي والدراسات العليا
كـليـــــــــــة العلـــــــــوم
ماجستير العلـــــــوم الحياتيـــــة
تحاليـــــــــل طبيـــــــــــة

Clinical and Dietary Assessment of Chronic Type-II Diabetic Patients in Gaza Governorate

التقييم السريري والغذائي لدى مرضى السكري المزمن من النوع الثاني في محافظة غزة

Maysa R. Abu El-Khair

Supervisor:

Prof. Baker mahmoud Zabot
Prof .of Nutrition, and Biochemistry

A thesis submitted in fulfillment of the requirements for the master degree in Medical Technology

Oct/ 2017

إقـــــرار

أنا الموقع أدناه مقدم الرسالة التي تحمل العنوان:

Clinical and Dietary Assessment of Chronic Type-II Diabetic Patients in Gaza Governorate

التقييم السريري والغذائي لدى مرضى السكري المزمن من النوع الثاني في محافظة غزة

أقر بأن ما اشتملت عليه هذه الرسالة إنما هو نتاج جهدي الخاص، باستثناء ما تمت الإشارة إليه حيثما ورد، وأن هذه الرسالة ككل أو أي جزء منها لم يقدم من قبل الآخرين لنيل درجة أو لقب علمي أو بحثي لدى أي مؤسسة تعليمية أو بحثية أخرى.

Declaration

I understand the nature of plagiarism, and I am aware of the University's policy on this.

The work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted by others elsewhere for any other degree or qualification.

Student's name:	**Maysa R. Abu El-Khair**	اسم الطالب:
Signature:		التوقيع:
Date:	2017/08/22	التاريخ:

بسم الله الرحمن الرحيم

الجامعة الإسلامية غزة
The Islamic University of Gaza

عمادة البحث العلمي والدراسات العليا هاتف داخلي: ١١٥٠

الرقم: ج س غ/٣٥/ Ref:

التاريخ: ٢٠١٧/٠٩/١٣م Date:

نتيجة الحكم على أطروحة ماجستير

بناءً على موافقة عمادة البحث العلمي والدراسات العليا بالجامعة الإسلامية بغزة على تشكيل لجنة الحكم على أطروحة الباحثة/ **ميساء رضوان سعدو أبو الخير** لنيل درجة الماجستير في **كلية** *العلوم* قسم **العلوم الحياتية- تحاليل طبية** وموضوعها:

التقييم السريري والغذائي لدى مرضى السكري المزمن من النوع الثاني في محافظة غزة

Clinical and Dietary Assessment of Chronic Type-II Diabetic Patients in Gaza Governorate

وبعد المناقشة التي تمت اليوم الاثنين ١٨ محرم ١٤٣٩هـ، الموافق ٢٠١٧/١٠/٠٩م الساعة الحادية عشرة صباحاً، اجتمعت لجنة الحكم على الأطروحة والمكونة من:

أ.د. بكـــر محمـــود الزعبـــوط	مشرفاً و رئيساً	.....
د. فـايز عبـد الـرؤوف المبحـوح	مناقشـاً داخليـاً	.....
د. نهـــاد رفيـــق اليـــازجي	مناقشـاً خارجيـاً	.....

وبعد المداولة أوصت اللجنة بمنح الباحثة درجة الماجستير في **كلية** *العلوم*/ قسم **العلوم الحياتية - تحاليل طبية**.

واللجنة إذ تمنحها هذه الدرجة فإنها توصيها بتقوى الله تعالى ولزوم طاعته وأن يسخر علمها في خدمة دينها ووطنها.

والله ولي التوفيق،،،

عميد البحث العلمي والدراسات العليا

أ.د. مازن اسماعيل هنية

Abstract

Clinical and dietary assessment of chronic type-II diabetic patients in Gaza Governorate

Background: Diabetes mellitus is a metabolic disease characterized by hyperglycemia occurs when the pancreas cells produce insufficient amounts of insulin hormone.

Objective: To assess of the clinical and dietary status of chronic T2DM patients in Gaza Governorate.

Subjects and Methods: study design was a cross-sectional which was employed among 100 patients (50 males & 50 females) with new diagnostic T2DM from primary health centers Gaza Governorate. Biochemical parameters and HbA1c were examined. Patients were asked to fill out a questionnaire to identify factors associated with poor glycemic control by conducted using SPSS software version 23.

Results: The prevalence of poor controls was 64% among Type II diabetes mellitus (T2DM) patients. Poor controls were significantly associated with education levels, smoking, physical activity, and income, economic levels, increase BMI, Family history of T2DM, bean and candy intake. The level of glucose, HbA1c, kidney and liver function, total cholesterol (TC), Low density lipoprotein cholesterol (LDL-C) and triglyceride (TG) among patient with poor controls was higher statistically significant than good controls. In contrast, there was a significant drop in High density lipoprotein cholesterol (HDL-C) level in T2DM. HbA1C was having the positive significant correlation with glucose, TG and AST and negative significant with uric acid ($P<0.05$).

Conclusions: Poor control of HbA1c was observed among T2DM patient associated with education, smoking, physical activity, economic levels, increase BMI, bean, and candy.

Keywords: clinical, dietary status, T2DM, Poor controls, Gaza Governorate.

التقييم السريري والغذائي لدي مرضى السكري المزمن من النوع الثاني في محافظة غزة

المستخلص

المقدمة: داء السكري من النوع الثاني هو عبارة عن مجموعة من الأمراض الأيضية التي تتميز بارتفاع مستوى السكر في الدم وذلك يحدث عندما ينتج البنكرياس كميات غير كافية من هرمون الأنسولين أو أن أنسجة الجسم تصبح مقاومة لزيادة مستوى هرمون الأنسولين.

الهدف من الدراسة : تقييم الحالة السريرية والحالة الغذائية لداء السكري من النوع الثاني المزمن في محافظة غزة.

الطرق والأدوات: البيانات المستخدمة في الدراسة تم الحصول عليها من خلال المقابلة المباشرة مع المرضى داء السكري من النوع الثاني حيث تشمل الدراسة 100 من المرضى المشخصين الجدد والمراجعيين لأربع مراكز رعاية أولية في غزة. تم فحص مخزون السكر والمعايير البيوكيميائية للمرضى واستخدام الحزمة الإحصائية SPSS-23 لتحليل البيانات.

النتائج: كان نسبة المرضى الذين يعانون من زيادة في مخزون السكر عن الحد الطبيعي 64٪. وأظهرت الاختبارات الإحصائية وجود علاقة ذات دلالة إحصائية بين ارتفاع مخزون السكر وكل من انخفاض مستوى التعليم وانخفاض مرات التماريين الرياضية وانخفاض مستوى الدخل وارتفاع نسبة التدخين، وزيادة مؤشر كتلة الجسم تناول الأطعمة مثل الفول والحلويات التاريخ العائلي للمرض. أما بخصوص المعايير البيوكيميائية مثل مستوى الجلكوز، ووظائف الكلى والكبد والكولسترول والدهون الثلاثية والكولسترول منخفض الكثافة، بدلالة إحصائية وجد أنه بالنسبة للمرضى الذين يعانون من ارتفاع مخزون السكر أعلى من الناس الذين لا يعانون بالمقابل كان الكولسترول مرتفع الكثافة منخفض في المرضى الذين يعانون من ارتفاع مخزون السكر مقارنة بمن لديهم مخزون السكر طبيعي. وأبرزت النتائج أن مخزون السكر يتناسب تناسب طردي ذو دلالة إحصائية مع مستوى السكر في الدم والدهون الثلاثية و احدى وإنزيمات الكبد (AST)، وعلاقة عكسية بين مخزون السكر و حمض اليوريك.

الاستنتاجات: زيادة مخزون السكر مرتبط بمستوى التعليم، والتدخين، والنشاط البدني والدخل، ، زيادة مؤشر كتلة الجسم والتاريخ العائلي للمرض والأطعمة مثل البيقوليان والحلوى وأن هذه الزيادة في مخزون السكر تعتبر مؤشر للعديد من المضاعفات مثل أمراض القلب، واعتلال بعض أعضاء الجسم ومن أهمها الشبكية، والأعصاب، والكلى والكبد.

الكلمات المفتاحية: داء السكري من النوع الثاني، مخزون السكر، التقييم السريري والغذائي، محافظة غزة

Dedication

To my parents,
brothers and sisters who have always
supporting me
To my husband who supported me
along the time
To my children
To researchers who are working to
improve the quality of life
To all of them I dedicate this work

Maysa R. Abu ElKhair

Acknowledgment

Would like to highly thank:

My supervisor **Dr. Baker mahmoud Zabut** Prof .of Nutrition & Biochemistry, Faculty of Science in Biochemistry Department at The Islamic University of Gaza (IUG) for his inspiration, guidance, and true commitment to my research.

The Islamic University of Gaza and the Faculty of Science for giving me the knowledge & opportunity to achieve my research

All the colleagues & staff members of Medical Technology Master Program

All the laboratory staff members at laboratory General Administration of Primary Health Care in Ministry of Health (MOH) for their kind help.

All the staff of Directorate General of Human Resources Development .

Table of Contents

List of Tables

List of Figures

List of Annexes

List of Abbreviations

ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BMI	Body mass index
BSA	Body surface area
CKD	Chronic kidney disease
CVD	Cardiovascular disease
DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
ESRD	End stage renal disease
FPG	Fasting plasma glucose
GDM	Gestational diabetes mellitus
GFR	Glomerular filtration rate
GIP	Glucose dependent insulinotropic peptide
GLP-1	Amylin, glucagon like peptide-1
Hb A1C	Glycated hemoglobin
HDL-C	High density lipoprotein cholesterol
high-GI	High glycemic-index
IDDM	Insulin dependent diabetes mellitus
IDF	International diabetes federation
IFG	Impaired fasting glucose
IGH	Impaired glucose homeostasis
IGT	Impaired glucose tolerance
LA	Lactic acidosis
LDL-C	Low density lipoprotein cholesterol
low-GI	Low glycemic-index
MI	Myocardial infarction
n	Number
NPDR	Non- proliferative diabetic retinopathy
OGTT	Glucose tolerance test

P	Probability
PDR	Proliferative diabetic retinopathy
r	Correlation
RGT	Renal glucose threshold
SD	Standard deviation
SGLT1	Low capacity sodium glucose cotransporter-1
SGLT2	Sodium glucose cotransporter-2
SPSS	Statistical Package for Social Sciences
t	Student t test
T1DM	Type I diabetes mellitus
T2DM	Type II diabetes mellitus
TG	Triglycerides
VLDL	Very low density lipoproteins
WHO	World health organization.
χ^2	Chi square test

Chapter 1

Introduction

Chapter 1
Introduction

1.1 Overview

Diabetes mellitus (DM) is of a metabolic diseases characterized by elevated in glucose levels resulting from defects in insulin mechanism, insulin hormones secretion, combined by both. Two type of forms of DM were identified; type I (dependant) and type II (independent). Severe reduction or no secretion of insulin hormones due to viral infections or autoimmune complications of beta cells in the pancreas is considered type I diabetes, which accounts for 6-10 % of DM patients. The most common form, T2DM, accounts for about 90% of cases DM (American Diabetes Association, 2014). T2DM usually begins as insulin disorder or resistance in which the cells in tissue do not use insulin properly. As the need for insulin rises, the pancreas gradually loses its ability to reduce it (Odegaard, 2013). T2DM has become main of the most important chronic public health problems in the word (Shaw, Sicree & Zimmet, 2010).

Lack of insulin hormones secretion or insulin action in T2DM incite glucose in hepatic output by stimulating glycogenolysis, decrease glycogen synthesis and gluconeogenesis then elevated rates of glucose production in hepatic cells to the development of overt increase glucose levels, especially fasting hyperglycemia (Rui, 2014). In such cases, adipose tissue induces lipolysis leading to increasing free fatty acids levels in the blood. On the other hands, excess free fatty acids in the blood of DM are converted into cholesterol & phospholipids in the hepatic cells. These two substances along with excess TG formed at the same time in the hepatic cells may be discharged into the plasma in the form of lipoproteins (Chapman et al., 2011). However, disturbance in hepatic and renal cells functions was also reported in T2DM (Atiba et al., 2013).

Life style elements and dietary are central to the prevention of T2DM and decrease complications. Last studies have recommended and that the consumption of dietary factors with low omega 6 polyunsaturated fatty acids (FA), and elevated trans unsaturated FA with elevated T2DM risk, but the role of

omega3 fats remains not appear (Wu et al,2011). Saturated fat acid intake was associated with higher risk of T2DM but these not associations with BMI. The increase in consumption of processed meats may be elevated the risk of T2DM. (Astrup et al, 2011). Intake large amount of dietary food, especially of the soluble type, improves glycemic control, drop on hyperinsulinemia, and decrease lipid in blood in T2DM (Ye et al, 2012).

1.2 General objective

To assess the clinical and dietary status of chronic T2DM patients among Gaza Governorate.

1.3 Specific objectives

1. To estimate whole blood HbA1C, serum glucose.
2. To determine BMI, dietary data, life style and risk diabetic complication among good and poor controls.
3. To measure lipid profile including cholesterol (ch), TG, low-density lipoprotein cholesterol (LDL-C) & high-density lipoprotein cholesterol (HDL-C) among T2DM good and poor controls.
4. To test liver function throughout measurement of aspartate aminotransferase (AST) & alanine aminotransferase (ALT) among good and poor controls.
5. To examine urea, creatinine and uric acid throughout estimation, urea and uric acid among good and poor controls.
6. To determine significant correlations between HbA1c, Glucose & BMI among previous parameter.

1.4 Significance

1. In Gaza Governorate, diabetes is epidemic degree 9% and clinical and dietary assessment for poor controls represents one of the major complications developed T2DM patients as they have more than five times greater risk for developing complication than good controls persons, which is a common cause of renal disease, cardiovascular disease (CVD), neuropathy, retinopathy and others complications.
2. In the Gaza Governorate a lot of studies for T2DM (AbuMustafa and Yassin, 2017; Elsous, Radwan, Al-Sharif& & Mustafa, 2017; El Bilbeisi, Hosseini& Djafarian, 2017). However clinical and dietary assessment for poor controls in T2DM has never been investigated in Palestinian diabetic patients. This will be the first study to assess clinical and dietary assessment for poor controls among T2DM in Gaza Governorate.
3. Early detection of poor monitoring of blood glucose level delays diabetic complications progression before the onset of clinical symptoms, thereby leading to increased survival and lower treatment costs.
4. Understanding the dietary style in poor controls patients among T2DM may be helpful in the control of diabetic complication.

Chapter 2

Literature Review

Chapter 2

Literature Review

2.1 History and definition of DM

DM is metabolic disorder characterized by chronic increase glucose resulting from defects in insulin hormones action and insulin secretion or both. DM was in past minor significance to world health, but now consider one of the main problems for human health in this century. The past two decades have seen an explosive elevated in the number of people diagnosed with DM. Pronounced changes in the human environment, and in human life style & behavior, have accompanied globalization, and these have resulted in escalating rates of DM (American Diabetes Association, 2014).

Insulin hormone is a peptide secreted from pancrease especially in the beta cells of the islets of Langerhans and have a function for controls levels of normal blood glucose by induce regulating carbohydrate, lipid, protein metabolism, cellular glucose uptake, and cell division and growth (Nakamura, Yudell & Loor, 2014).

Renal is an important organ to the contributor in the regulation of glucose levels (plasmatic glucose levels) (Peng, 2015). The glomerulus filters about 162 grams of glucose/day from blood, all of glucose which is reabsorbed in renal under normal status (Jaikumkao et al., 2017).

In fact, avoided urinary glucose loss by the kidney to prevent energy loss and kidney tubular cells have the ability to induce glucose reabsorption capacity depending on glucose levels, this in turn depending on plasma glucose levels. however, high capacity sodium glucose cotransporter-2 (SGLT2), low capacity sodium glucose and high-affinity low affinity, cotransporter-1 (SGLT1), both located in the proximal tubule of the renal system, elevated their activity in presence of increased glucose load in tubular (Bonner et al., 2015).

It normal individuals, glomerular filtration rate (GFR/ mg/min per m^2 body surface area (BSA)) is 90 to 120, essentially complete glucose reabsorptive

capacity is maintained up to glucose plasma concentrations of about 11 mM. When blood glucose levels increase, transporters of glucose tubular consider saturated & urinary glucose excretion elevated. (Nishimura, et al., 2015). The blood glucose concentration at which this status is observed is called the renal glucose threshold (RGT) (Peters et al., 2015).

2.2 Risk factors for diabetes mellitus

The American Diabetes Association (ADA) recommends broader diagnostic criteria by targeting everyone age >45 as well as increase BMI adults of any age who have higher risk factors, including family history of DM, physical inactivity, high lipid levels, hypertension, being a member of a high risk racial people , signs of insulin receptors not response, polycystic ovarian syndrome (PCS), as well as previous diagnosis of preDM having (Dall et al., 2014).

2.3 Prevalence and mortality rate of DM

DM continues to elevate in terms of the number of affected and in the world and is a growing problem in public health. It is estimated that there were about 300 million people with DM in 2010, and this number is expected to increase proximately 450 million by 2030 (Shaw et al., 2010).

DM and its complications are big health problems in the occupied Palestinian territory according to all estimates. In 2000, the estimated prevalence rate of diabetes was 9.1% in adults aged ≥30 years. Routine data by the United Nations Relief and Works Agency illustrated the prevalence rate of DM was about 11% in the West Bank and 12% in the Gaza Governorate among the registered Palestinian refugees aged ≥40 years. The rate of reported DM was 7.0% at age 40–50 years, 19.1% at 50–60 years, and 25% at ≥90 years (Husseini et al., 2009).

The prevalence of diabetes rate in Palestine was estimated to be around 10% in a study conducted in 2000 in co-operation with Al-Quds University, Jerusalem. This rate is the same as that reported in others countries such as Egypt and Tunisia and is lower than Saudi Arabia (about 12%) and Oman (about 13%). In the Gaza Governorate, by the end of 2002, there were about 15,000 Palestinian

refugees with DM. The incidence rate of new cases among refugees people was about 250 per 100,000. About 19% of newly diagnosed people with DM were <30 years, 27% were between the age of 40-60 years, and 54% were >60 years. However, 26% of people with DM is higher in BMI than normal; and the newly study showing the prevalence of obesity among DM people in Gaza is 60%. (Tsapogas, 2004).

DM Mortality is difficult to define and screening. This disease caused about 3.0% of deaths in the total population i.e., about 8.5 /100,000 population in the occupied Palestinian territory. DM complications consider large health problems in the occupied Palestinian territory according to all last study (Husseini et al., 2009).

2.4 Classification of diabetes

The classification of DM is essentially derived from etiology and includes the pathophysiology staging based on the level of insulin hormones. These defects are classified into four groups: (1) T1DM; (2) T2DM; (3) gestational diabetes mellitus (GDM); and (4) impaired glucose homeostasis (IGH) and others rare types of diabetes due to causes do not match with major common types of DM (American Diabetes Association, 2017).

2.4.1 Type 1 diabetes mellitus (T1DM)

T1DM is occurred when the immune system damage the insulin-producing beta (β) cells in the pancreas by an autoimmune disease that stop regulate blood glucose levels. The immunologic diseases that lead to T1DM can begin years before the symptoms of T1DM develop. T1DM mostly has an acute onset, with adolescents & children usually able to pinpoint when symptoms began. Symptoms will be apparent when most of the beta-cell of pancreas destroyed. The mean age of the diagnosis of T1DM is 12 years (Kaufman, Gallivan & Warren-Boulton, 2009).

First symptoms, mainly due to elevated blood glucose, include urination and increased thirst, constant feeling hunger, increase weight loss and not a clear

vision. However, patients also may fatigue and insulin hormones deficiency worsens, ketone bodies (formed from the breakdown of fat) build up in the blood and are excreted in the breath and urine. They cause worsening dehydration, a decrease of breath, vomiting and abdominal pain, and. Elevation of blood glucose, acidosis and dehydration comprise the condition known as diabetic ketoacidosis (DKA). If diabetes is not treated with insulin at this point, the individual can death by diabetic coma. It is common for children with vomiting to be missing diagnosed as having gastroenteritis. New cases of diabetes can be differentiated from gastrointestinal infections by the increase occurrence urination that accompanies with vomiting DM diabetes (Kaufman et al., 2009).

2.4.2 Type 2 diabetes mellitus (T2DM)

T2DM develops when insulin hormones production by beta cells decreases following a prolonged period of hyper insulinemia hormones. The term pancreatic exhaustion of pancreatic insufficiency is used to describe this process of decomposition. In T2DM, the pancreatic insulin hormones secretion lowing as a result of direct destruction to the pancreas and loss of beta cell mass (Frank and Tadros, 2014).

Prevalence of T2DM Accounts about 90 to 95% of all diagnosed cases of DM. Most patients with DM have higher BMI than normal (obese), and overweight itself causes some degree of insulin resistance. T2DM patients who are not obese by traditional weight criteria may have an elevated percentage of body fat distributed in the abdominal area. DKA rarely occurs spontaneously in T2DM; when seen, it usually arises in association with the depression of another illness such as infection. This form of diabetes frequently goes not screening for many years because the increase glucose levels develop gradually and at earlier stages is often not severe enough for the patient to notice any of the classic symptoms of DM. However, such T2DMpatient have increased the risk of developing cardiovascular disease (CVD) complications (American Diabetes Association, 2014).

Insulin mediates its actions through binding to insulin hormones receptors. It consists of a heterotetramer consisting of 2 alpha and 2 beta glycoprotein subunits linked part by disulfide bonds and is present on the cell membrane of cells. Insulin hormones bind to the extracellular alpha subunit, resulting in conformational change enabling ATP to bind to the intracellular component part of the beta subunit. ATP binding, in turn, triggers phosphorylation of the beta subunit conferring tyrosine kinase (TK) activity. This enables tyrosine phosphorylation (TPh) of intracellular substrate proteins known as insulin responsive substrates (IRSs). The IRS will be bind other signaling molecules that mediate further cellular actions of insulin hormones (Yoneyama et al., 2013). The pathways and influences of insulin hormones secretion are presented schematically in Figure 2.1.

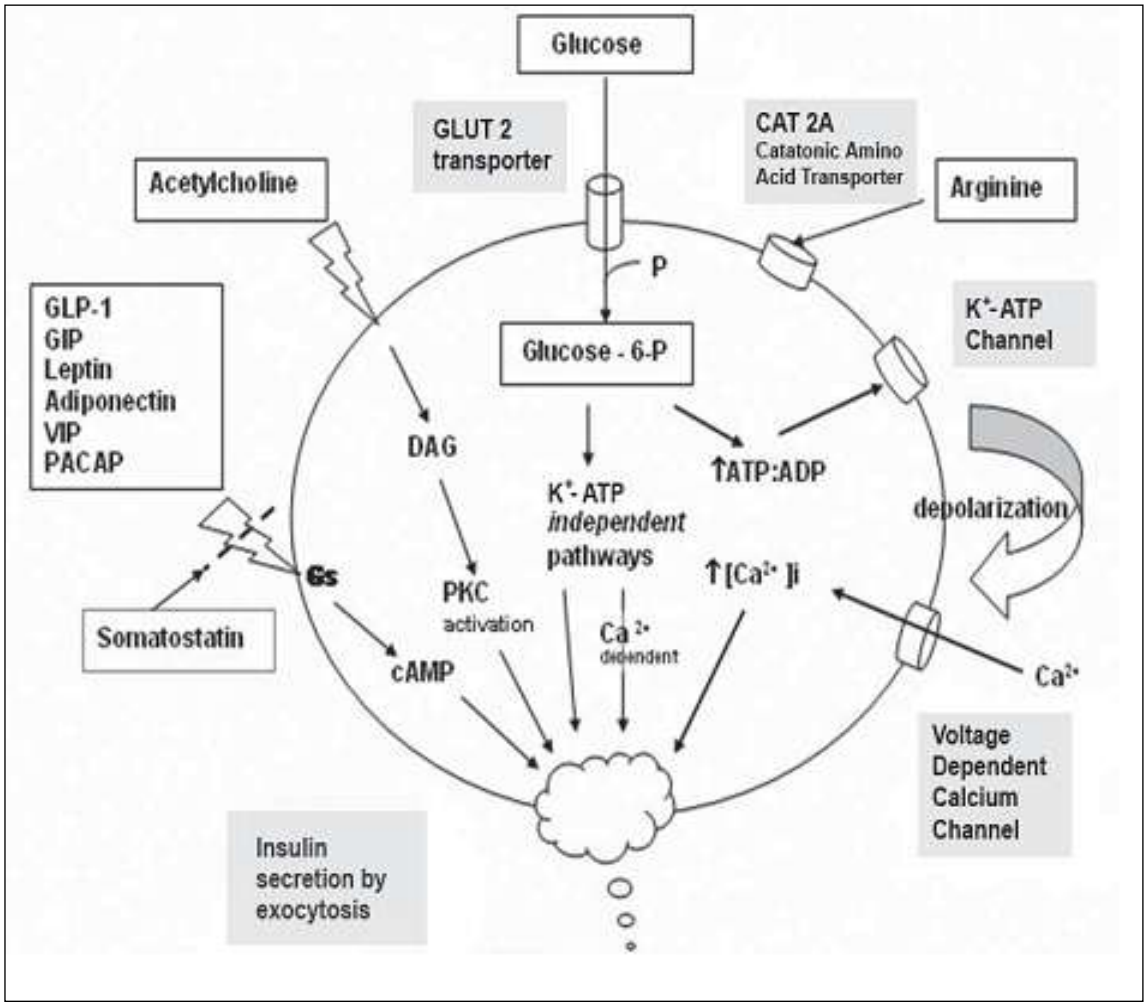


Figure (2.1): Schematic representation of insulin secretory pathways

Source: (Wilcox, 2005)

Blood glucose concentration indicates to the rate of glucose levels entering the blood circulation balanced by the rate of glucose removal from the blood circulation. Circulating blood glucose is derived from three sources: (1) absorption of intestinal during the fed state, (2) glycogenolysis, and (3) gluconeogenesis. The big determinant of how quickly glucose appears in the blood circulation during the fed state is the rate of gastric emptying. Other sources of circulating glucose are derived chiefly from liver processes: glycogenolysis, the breakdown of glycogen, the polymerized storage form of glucose; and gluconeogenesis, the formation of glucose primarily from amino acids and lactate during the fasting state (Sharabi, Tavares& Rines & Puigserver, 2015).

Glycogenolysis & gluconeogenesis are essecianal the control of glucagon, a hormone produced in the cells of the pancreas. During the first 8–12 hours of fasting, glycogenolysis is the primary mechanism by which glucose is made available. Glucagon facilitates this process and thus promotes glucose appearance in the circulation. Over longer periods of fasting, glucose, produced by gluconeogenesis, is released from the liver (Dash et al., 2017).

The amount of glucose entering the blood circulation balanced by the amount of glucose removal from the blood circulation. The glucose regulatory hormones of the human body are designed to maintain blood circulating glucose in a relatively narrow normal range. glucose regulatory hormones include hormones decrease glucose in blood circulation (insulin hormones) , and others decrease glucose in blood circulation such as glucagon, epinephrine, glucagon-like peptide-1 (GLP-1), cortisol & growth hormone of these, insulin and amylin hormones are derived from the beta cells of the pancreas, glucagon hormones from the alpha cells of the pancreas, and GLP-1 hormones from the L-cells of the intestine (Wewer, et al., 2017).

In the bi-hormonal action of blood glucose levels homeostasis, insulin hormone is the key regulatory of removal glucose of blood circulation, and glucagon is a

regulator of elevated glucose levels. After reaching a post-meal peak, plasma glucose level slowly drops during the time, finally returning to fasting blood glucose levels. In the first post-feeding state, glucose removal into adipose and muscle tissue is driven mainly by insulin hormones. At the same moment, endogenous glucose production is suppressed by 1) the direct action of insulin on the hepatic cells, and 2) the paracrine effect or direct communication within the alpha- and beta- pancreas cells, which results in glucagon secretion suppression (Vidanelage & Jayasinghe, 2013).

2.4.3 Gestational diabetes mellitus (GDM)

GDM is blood glucose intolerance of variable severity with the onset of primary recognition at beginning pregnancy (WHO, 2015). increase glucose levels during pregnancy is found to be associated with various perinatal & maternal adverse outcomes (Landon et al., 2011). Their outcome will have a life-long increase risk of glucose intolerance, metabolic syndrome, high and overweight, whereas the mothers of the fetus will have a higher risk of metabolic syndrome and DM in the future (American Diabetes Association, 2014).

The screening of GDM during mother's pregnancy provides an opportunity to diagnostic and prognostic women with risk of long term and short term GDM complications. It has been shown that early screening and intervention can decrease the adverse perinatal outcomes (Horvath et al., 2010).

2.4.4 Impaired glucose homeostasis (IGH)

IGT is defined as a metabolic stage intermediate between normal glucose DM and homeostasis. IGH have two subgroups (Nathan et al., 2007).

a) Impaired Fasting Glucose (IFG): Fasting plasma glucose (FPG) elevated than normal blood glucose levels (110 - 125 mg/dl), and less than screening DM test (< 140 mg/dl).

b) Impaired Glucose Tolerance (IGT): Blood glucose upper normal, and lower screening test, following administration of blood glucose load of 75 gm, (≥ 140 and lower than 200 mg/dl).

2.4.5 Other specific types of diabetes mellitus

There are other types of DM secondary to rare cases do not match with T1DM, T2DM, IGT and GDM (Sollu et al., 2010) such as:

1) Genetic defects of the pancreatic beta cells

These associated with a monogenetic problem in the beta cells function. They are referred to as maturity onset DM of the young and are defined by impaired insulin hormones production with minimum or no problem in insulin action.

2) Genetic defects for insulin hormones receptor

These are defect associated with mutations of the insulin hormones receptor and may range from increase production of insulin and modest increase blood glucose levels to severe DM.

3) Exocrine pancreas diseases

Any process or defect that causes injure the pancreas cells can cause DM. Acquired causes such as microbial infection, trauma in pancreas, pancreatitis, and pancreatectomy

4) Endocrinopathies

Defect that results from excess growth hormone (acromegaly), Cushing's syndrome (high levels of cortisol), a tumor of the alpha cells (glucagonoma), and pheochromocytoma can all cause DM.

5) Chemical and Drug -induced DM

This phenomenon of DM occurs with chemicals or drugs that affect on insulin hormones production, increase insulin hormones saturated receptors or permanently defect pancreatic beta cells, as is seen with the administration of an elevated dose of steroids hormones. Corticosteroids hormones have effects on glucose metabolism: stimulating the hepatic cells to produce glucose from lipids and proteins. In the periphery, corticoids lowering glucose utilization elevated amino acid productions and induce lipolysis, thereby providing lipid and amino

acids from gluconeogenesis. The net result elevated in plasma glucose levels immediately.

6) Infections

Viral and some bacterial infections that may cause pancreatic beta cell destroy include hepatitis B virus, mumps, adenovirus, and CMV.

7) Genetic syndromes

Sometimes genetic syndromes associated with DM such as syndrome, Turner's syndrome, Wolfram syndrome and Down's syndrome

2.5 Symptoms and Signs of DM

Symptoms of DM often goes undetected because DM can be attributed to many other causes and no symptoms for some patients experience or fail to heed warning signs.

Possible indicators of DM **(Samreen, 2009)** such as:

- Polydipsia
- polyuria
- dehydration
- Excessive appetite
- Unexplained decrease of BMI
- vision problems
- nearsightedness
- infections
- Slow healing of injury
- Skin problems
- Fatigue
- Shakiness
- Mood swings
- Dizziness

2.6 Screening test of DM

The screening test of DM is established by increase blood glucose levels. For a long time, the only method recommended for screening test was a direct demonstration of elevated blood glucose concentrations. In last 1979, a set of criteria base on the distribution of blood glucose in high-risk populations was established to standardize the screening test. These recommendations had agreement by the WHO **(National Diabetes Data Group, 1979)**. In 1997, the

screening test of DM is established by increase blood glucose levels. For a long time, the only method recommended for screening test was a direct demonstration of elevated blood glucose concentrations. In 1980, a set of criteria base on the distribution of blood glucose in high-risk populations was established to standardize the screening test. These suggested were have an agreement by the WHO criteria were modified to better diagnostic test for individuals at risk of nephropathy & retinopathy (Engelgau et al., 1997). The revised criteria comprised:

1) An FPG value ≥ 126 mg/dL
2) 2-hour postprandial test concentration ≥ 200 mg/dL
3) Symptoms of DM and a casual (i.e., regardless of the time of the preceding meal became blood glucose concentration > 200 mg/dL).

If any patients have one of these three screaming test is met, confirmation must be by retest on a subsequent day is important to establish the screening test. International Diabetes Federation & WHO recommend either a 2-hour postprandial test or FPG test that uses the same cutoffs as the American Dental Association (WHO, 2006). The International Expert Committee recommended at 2009 that comprised members appointed by the International Diabetes Federation, American Dental Association and the European Association for the Study of DM, recommended that DM may be screening by the measurement of glycated hemoglobin A1c, that reflects long term (100 days) blood glucose levels. The WHO and the American Dental Association has endorsed the use of glycated hemoglobin A1c for the screening and diagnosis of DM (International Expert Committee, 2009).

Glucose in urine occurs when plasma glucose level exceeds roughly 180 mg\dl in an individual with normal kidney function. Glucose will be freely filtered in the glomerulus but is mostly will be completed reabsorbed in the renal proximal tubule. The filtrate of glucose in the urine may indicate to high blood glucose, resulting in a blood glucose load in the filtrate that increases the proximal kidney tubule's ability to reabsorb filter glucose. In fact, glucose does not filtrate in the urine until the Blood level became upper 180 to 200 mg/dL. However, glucose in

the urine may reflect a defect in the ability to reabsorb filtered glucose load by the proximal tubule kidney cells' a normal. When this defect occurrence is an isolated one, it is termed renal glycosuria and is due to a mutation in transporter such as SGLT2 (Van Bommel et al., 2017).

2.7 Criteria for the screening of DM

Diagnose or screening of DM was established by four ways that possible and each of these tests must be repeated testing on a different day by any one of the following methods that are summarized in Tables 2.1 and 2.2.

Table (2.1): Criteria for the diagnosis or screening of DM, any one of the following tests will be diagnostic DM **(**Sacks et al., 2011**).**

1	Symptoms of diabetes plus random (casual) plasma glucose concentration ≥ 200 mg/dl (11.1 mmol/l).
2	FPG ≥ 126 mg /dl (7.0 mmol/l).
3	2-hours PG ≥ 200 mg /dl (11.1 mmol/l) during an OGTT.
4	HbA1C ≥6.5%.

Table (2.2): reference **v**alues for screening and diagnosis of DM and another form of hyperglycemia **(Seino et al., 2010).**

Stage	FPG	Random PG	OGTT
Normal	FPG less than 110 mg/dl		2h-PG less than 140 mg/dl
Impaired glucose homeostasis	Impaired Fasting Glucose (IFG) = FPG ≥ 110 mg/dl and less than 126 mg/dl		Impaired Glucose tolerance (IGT) = 2h-PG ≥ 140 mg/dl and less than 200 mg/dl
Diabetes	FPG ≥ 126 mg/dl	≥ 200 mg /dl plus symptoms	2h-PG ≥ 200 mg/dl

2.8 Diabetes Mellitus complications

Complications of type 2 diabetes include acute and chronic complications. The acute complications comprise DKA, hyperosmolar hyperglycemic non-ketotic coma, lactic acidosis, and hypoglycemia. The chronic complications include cardiovascular disease, diabetic nephropathy, neuropathy and retinopathy (Parthiban et al., 2014). Other complications such as urinary tract infections (UTI), foot problems, some types of cancer, leg amputations, decreased cognitive abilities, skin damage, sexual dysfunction, pregnancy complications, bacterial and yeast infections, gingivitis, thrush, tuberculosis and other infections (Samreen, 2009).

2.8.1 Acute complications of DM

The acute metabolic complications of DM include:

1) Diabetic ketoacidosis (DKA)

DKA is an acute complication of DM with life threatening and included of the biochemical triad of increase blood glucose, metabolic acidosis, and ketone body in urine (Dhatariya et al., 2017). DKA is combined with the loss of electrolytes and dehydration, elevated potassium, increase blood acidity, and progressive loss of consciousness with inducing severe insulin hormones deficiency with increased counter-regulatory hormones levels (catecholamines, glucagon,

cortisol, growth hormone). The biochemical criteria for screening and diagnosis test are blood glucose more than 200 mg/dl, venous pH less than 7.3 or bicarbonate less than 15 mEq/L, ketonemia more than 3 mmol/L and the presence of ketone in urine (Savoldelli, Farhat & Manna, 2010).

DKA consider the most frequent cause mortality among T1DM adolescents and children, and its prevalence approximately fifty percentage of deaths among DM patients up to 24 years of age. Clearly, T2DM patients are susceptible to DKA under depression situations such as bacterial and yeast infections, trauma or surgery (Kamata et al., 2017). In developed countries, the mortality rate of DKA is 0.15 to 5% and it is major due to cerebral edema, occurring in approximately 1% of the cases (Farsani et al., 2017).

2) Hyperosmolar hyperglycemic non-ketotic coma

Hyperosmolar hyperglycemic non-ketotic coma is a state of elevated blood glucose, hyperosmolarity, and little or no ketosis. The most common causes of hyperosmolar hyperglycemic non-ketotic coma include medications non-compliance, undiagnosed diabetes and substance abuse (Khan, Iqbal Haider & Humayun, Khan, 2016).

3) Lactic acidosis (LA)

LA is very rare and that potentially threatening metabolic status that can occur whenever substantial cells hypoperfusion and decrease oxygen exist (Nishihama et al., 2017). LA is characterized by an increased blood lactate concentration that became more than 45.0 mg/dL or more than 5.0 mmol/L, lowering blood pH less than 7.35 with disturbances of electrolyte which induce increased anion gap (Stevens, et al., 2015).

LA is more prevalence in DM patients than healthy persons and because increase LA levels may occur in dangerous volume contracted patients, plasma lactate should be assess on admission (Fayfman, Pasquel & Umpierrez, 2017).

4) Hypoglycemia

Hypoglycemia is a main, potentially fatal self-complication of the treatment of DM patients. The risk of decrease blood glucose levels increases significantly with taken directed with pharmacologic therapy toward maintaining the glucose range as close to those found in the healthy subject as possible. It has been screening that blood glucose levels may be less than 50–60 mg/dl (Unger, 2012). fasting blood glucose levels can be useful for diagnostic asymptomatic hypoglycemia and allowing DM patients to avoid main hypoglycemic episodes (Tsirona et al., 2016)

2.8.2 Chronic complications of DM

Chronic complications are divided into two subgroups (1) macrovascular (affecting main arteries) and (2) microvascular (affecting small blood vessels).

1) Microvascular complications

a) Diabetic neuropathy

Diabetic neuropathy is a serious and common complication of DM. It has been estimated that up to 50% of patients with T1DM or T2DM will have the complication of neuropathy (Pop-Busui et al., 2017).

When the autonomic nervous system is affected, this can lead to a variety of symptoms such as tachycardia, orthostatic hypotension, gastroparesis, constipation, diarrhea, fecal incontinence, impotence and bladder dysfunction, thus significantly affecting the quality of life of DM patients. Furthermore, the presence of autonomic neuropathy carries a significantly elevated risk of cardio-vascular mortality. Deficits in the autonomic supply to the skin can also disrupt the microvascular flow and impair sweating, contributing to the development of foot ulcers that occur as a consequence of the sensory deficits related with sensory neuropathy in diabetes. Chronic foot ulcers that fail to heal are a major cause of non-traumatic amputation (Freeman, et al., 2013).

b) Diabetic retinopathy (DR)

DR is the main prevalence cause of new cases of blindness among adults aged. DR progresses from mild nonproliferative abnormalities, characterized by elevated vascular permeability with moderate and severe nonproliferative DR which characterized by vascular block, to proliferative diabetic retinopathy (PDR), characterized by the growth of new blood vessels on the retina of the eye and posterior surface of the vitreous of eyes. Macular edema that term to retinal thickensing from leaky vessels of blood, can prognosis at different stages of retinopathy. DM, pregnancy, puberty, hypertension, and cataract surgery can accelerate these changes (Yau et al., 2012).

First two decades of DM, approximately most patients with T1DM and ore than 60% of T2DM have retinopathy. In the Wisconsin Epidemiologic Study of DR, about 3.6% of younger onset type 1 diabetes and 1.6% of older onset patients with T2DM were legally blind. In fact, the younger onset group, about 85% of blindness was attributable to DR. In the older onset group which another's eye diseases were common, 33 % of the cases of legal blindness was due to DR (Tarr et al., 2013).

DR and maculopathy mostly progress and develop without any symptoms. Fundus screening tests are mandatory since only advanced stages cause Signs and symptoms which suggest the prognosis of DR are a sudden drop of visual acuity, a non-correctable drop of visual acuity. When the macula is affected: impaired color vision, impaired vision, blurred vision, "floaters" will be seen in front of the eye; these are, caused by tractive retinal detachments or vitreous hemorrhages (Hammes, Lemmen & Bertram, 2014)

c) Diabetic nephropathy (DN)

End stage renal disease (ESRD) is a common cause by DN (Alebiosu and Ayodel, 2005) and its related to a high mortality and morbidity (Astrup et al., 2005). DN prognosis due to a complex interaction between haemodynamic

pathophysiological factors and metabolic, which lead to kidney damage (Yamagishi, Okuda, Ueda & Fukami, 2007).

DN can affect about 25 % of the DM population, who present with an elevated in microalbuminuria in the earliest stage. This may development to macroalbuminuria and later ESRD. There is also evidence of an elevated in systemic and inflammation vascular markers (Kanasaki, Taduri, Koya & 2013) as the size of the renal progressively elevated (Satriano and Vallon, 2006). Accompanying these changes are abnormalities in the blood biochemical indices of kidney function, which precede chronic renal failure (Thompson, 2013).

Careful good control of glucose conditional minimizes the symptoms of DN indicating that increase blood glucose levels are the main driving force behind the development of DN (Lewko and Stepinski, 2009).

d) Infections

Bacterial and yeast infectious diseases are an associated with the source of mortality and morbidity in people with DM. The risk of macrovascular and microvascular complications associated with older age in DM patients and those complications are related to infection. Several defects in immune system also have been noted in DM patients (Shah and Hux, 2003).

Almost most infections occur by serious complications in DM patients include urinary foot ulcers, tract infections, pneumonia and necrotizing fasciitis. However, some type of infectious diseases occurs predominantly in DM patients, such as malignant otitis externa, emphysematous cholecystitis, and emphysematous pyelonephritis. Because these conditions can have serious complications, progress, and development rapidly, and fatal with prompt recognition and treatment is imperative. Good glucose levels control, early diagnostic for foot ulcers and educating DM patients about the care of the foot, and pneumococcus vaccination and influenza are critically important strategies for preventing infection (Chin-Hong, 2008).

2) Macrovascular complications (cardiovascular diseases)

Cardiovascular diseases (CVD) cause is about seventy percentage of death in people with T2DM. People with DM have a 4-time- greater risk to having a CVD event than people without DM after controlling for traditional risk factors for CVD, such as dyslipidemia, hypertension age, obesity, and tobacco use (Buyken et al., 2007).

CVD risk factors are predominant in DM, but data suggest that DM is an independent risk factor for CVD. Also, people with DM have a 5-time- risk for a primary myocardial infarction (MI) and a 2-time-greater risk for a recurrent MI than people who previously had an MI but do not have DM. These data suggest that the risk for an MI in people who have DM but who have not had an MI may be similar to that in healthy people but with a previous MI. However, people with diabetes have a poorer long-term development after an MI, including an elevated risk for congestive heart failure and death. Even people with insulin hormones resistance have an increased risk for CVD (Schramm et al., 2001).

2.9 Dietary and type 2 diabetic disease :

In the past couple of decades, a lot of cohort studies and clinical trials have converged to support the importance of individual dietary, foods, and nutrients patterns in the prevention and controls of type 2 diabetes. The quality of nutrients fats, proteins and carbohydrates consumed is more crucial than is the quantity of these macronutrients (Schwab et al., 2014). Diets rich in whole grains, fruits, vegetables, nuts, and legumes; alcohol consumption; and lower in refined grains, red or processed meats, and sugar-sweetened beverages have been shown to reduce the risk of diabetes and improve glycaemic control and blood lipids in patients with diabetes (Ley, Hamdy, Mohan &Hu, 2014). With an emphasis on overall diet quality, several dietary patterns such as Mediterranean, low glycaemic index, moderately low carbohydrate, and vegetarian diets can be tailored to personal and cultural food preferences and appropriate calorie needs for weight control and diabetes prevention and management. Although much progress has been made in development and implementation of evidence-based nutrition recommendations in developed countries, concerted worldwide efforts and policies are

warranted to alleviate regional disparities (Jannasch, Kröger, & Schulze, 2017; Micha et al., 2017).

Some studies have shown total and saturated fat intake was associated with a higher risk of T2DM, but these associations were not independent of BMI. Frequent consumption of processed meats may increase the risk of type 2 diabetes. Few studies have examined the possible role of n-3 fatty acids or trans- in the development of T2DM. Previously, we reported that trans-fat was positively associated and polyunsaturated fat inversely associated with risk of type 2 diabetes in women (Wedick et al., 2012; Chen et al., 2016; Xu et al., 2017).

Meat intake was associated with a higher risk of diagnosed diabetes in a study in Seventh-Day Adventists but it has never been examined in detail. In epidemiologic studies, intake of long-chain omega-3 fatty acids was associated with better glucose tolerance in some studies but not in others. Some intervention studies have found that omega-3 intake resulted in an increase in glycated hemoglobin (Hb A1C) and in fasting blood glucose (Kashiwagi et al., 2017). Epidemiologic studies of the relation of long-chain fatty acid intake with T2DM have reported conflicting results (Wanders et al., 2017).

Furthermore, because studies have suggested that environmental contaminants such as dioxins, found in fish, might raise the risk of T2DM, the risks and benefits of fish intake remain controversial (Samsom, Trived, Orekoya, & Vyas, et al., 2016). Another finding evaluated the role of dietary fiber on glycemic control in patients with type 2 diabetes were inconsistent. In some of the studies, the lack of control for concomitant changes in the intake of macronutrients makes the data difficult to interpret. For example, in the study Den Besten et al., (2015) and in that Chandalia, et al., (2000) shown the high-fiber diet had a lower fat and higher carbohydrate content than the low-fiber diet.

2.10 Dietary and controls in type 2 diabetes

To investigate the relationship between Dietary and controls type 2 diabetes, Wolever et al., (2008) were studied subjects with T2DM managed by diet alone (n = 162) were randomly assigned to receive high-carbohydrate, high-glycemic-index (high-GI), high-carbohydrate, low-glycemic-index (low-GI), or low-carbohydrate, high-monounsaturated-fat (low-CHO) diets for 1 years. They concluded in subjects with T2DM managed by diet alone with optimal glycemic control, long-term HbA1c was not affected by altering the GI or the amount of dietary carbohydrate. also, differences in total: HDL cholesterol among diets had disappeared by 6 mo. However, because of sustained reductions in postprandial glucose and CRP, a low-GI diet may be preferred for the dietary management of T2DM.

Effect of low glycemic load diet on glycated hemoglobin (hba1c) in poorly-controlled diabetes patients were estimated in hundred poorly-controlled diabetes patients, HbA1c > 8, age 52.8 ± 4.5 y, were administrated a low glycemic load (Low GL) = 67 (Energy 1800 kcal; total fat 36%; fat derived from olive oil and nuts 15%; carbohydrate 42%; protein 22%) for 10 weeks. They found positive moderate correlation between HbA1c concentration before intervention and FBS reduction after intervention ($P < 0.001$, at 0.01 level, $R = 0.52$), and strong positive correlation between FBS before intervention and FBS reduction ($P < 0.001$, at 0.01 level, $R = 0.70$). The authors demonstrated that our alternative low glycemic load diet can be effective in glycemic control (Ziaee, Afaghi & Sarreshtehdari, 2012).

Takahashi et al., (2016) studied Effects of total and green vegetable intakes on HbA1c and triglycerides in elderly patients with T2DM among the Japanese Elderly for 417 male type 2 diabetic patients aged 65 years or older enrolled in the Japanese Elderly Diabetes Intervention Trial. Dietary intakes were measured by using the Food Frequency Questionnaires method. The authors were concluded daily total vegetable intake of 200 g or more, and green vegetable intake of 70 g or more correlated with improved control of HbA1c and triglyceride levels in elderly type 2 diabetes patients through achieving a well-balanced diet.

Kollannoor, Shebl, Hawley & Pérez-Escamilla (2016) investigated whether there is associated with nutrition facts panel with higher diet quality and lower glycated

hemoglobin concentrations. they examined the association between food label use and glycated hemoglobin (HbA1c) concentrations. they conclusion In participants with undiagnosed prediabetes, the use of health claims alone, of both labels, or of neither label (compared with the use of the NFP only) was associated with poorer diet quality. In addition, users of neither label and users of both labels had poorer glycemic control. Further studies are needed to understand why the use of health claims may not be health promoting in this high-risk population.

The fiber in diet and improvement of glycated hemoglobin and lipid profile in patients with type 2 diabetes was studied as a cross-sectional survey of 395 patients with type 2 diabetes. and the study shown higher fiber intake was associated with a low HbA1c, high HDL-c levels, low weight, and waist circumference. The highest tertile of calories consumption was associated with a higher fasting glucose level and weight. The highest tertile of carbohydrate consumption was associated with a lower weight. The lowest tertile of total fat and saturated fat was associated with the highest tertile of HDL-c levels, and lower saturated fat intake was associated with lower weight and the authors demonstrated A higher content of fiber in the diet reduces HbA1c and triglycerides while improving HDL-c levels. Increasing fiber consumption while lowering calorie consumption seems to be an appropriate strategy to reduce body weight and promote blood glucose control (Velázquez-López et al., 2016).

Dietary fiber for the treatment of T2DM was assessed by Post, Mainous, King & Simpso, (2016). they suggest that increasing dietary fiber in the diet of patients with type 2 diabetes is beneficial and should be encouraged as a disease management strategy.

Higher-protein diets have been advocated for body-weight regulation for the past few decades. However, the potential health risks of these diets are still uncertain. We found a positive association between the protein score and eGFR in Lifelines (slope 0.17 ± 0.02 mL/min/1.73 m^2, $p < 0.0001$). The study suggested protein scoring might be a useful tool to assess both the effect of quantity and source of protein on health parameters (Møller et al., 2016).

Chapter 3

Materials and Methods

Chapter 3

Materials and Methods

3.1 Study design

The present study is cross-sectional**.**

3.2 Target population

The target population was T2DM aged 40-60 years from diabetic clinic centers in Gaza Governorate.

3.3 Sample size

The Sample size was 100 new diagnostic cases (50 males and 50 females) served as Patients were matched for age.

3.4 Sampling

A total of 100 new diagnostic cases (50 males and 50 females) blood samples were collected from T2DM patients (duration of T2DM is 3 – 6 years), which were previously screening and diagnosed according to the current WHO diagnostic criteria for DM (World Health Organization, WHO, 2006), from three DM clinic centers (El-remal, El-Sourani & El-Sheikh Radwan) in Gaza Governorate. The HbA1c is an accurate method to test the glycemic control over a preceding three months period. The present study divided in tow groups, first, higher HbA1c than the golden standard (>7%) means poor glycemic control and second, control HbA1c than the golden standard (≤7%) means good glycemic control **(American Diabetes Association, 2014).**

3.5 Exclusion criteria

- Type 1 diabetic patient.
- diagnostic cases more less than 3 years and more than 6 years
- Patients having the deferent therapies.
- Aged < 40 years and > 60 years

3.6 Ethical consideration

The necessary approval to conduct the study was obtained from Helsinki committee in the Gaza Governorate (Annex 3). Coordination with the Ministry of Heath was fulfilled (Annex 2).

3.7 Data collection

3.7.1 Questionnaire interview

A meeting interview was used for filling in the questionnaire which designated for matching the study need. All interviews were conducted face to face by the researcher himself. The questionnaire (Annexes 1) included questions on the personal profile of the study population (Age, gender and education), socioeconomic data (employment, family income, family history of diabetes and smoking), physical activity , diet, duration of diabetes, monitoring of blood glucose , dietary frequency per day, and self-reported complications (retinopathy, cardiovascular disease and neuropathy) among the study population and type of treatment .

3.7.2 Body mass index

Body mass index (BMI) was calculated as the ratio of body weight in Kg/height in meter square. The subjects were asked to remove shoes and heavy clothes before measurement of weight and height. The participant with BMI=18.5–24.9 kg/m^2 were considered to have normal weight, Participants with BMI=25.0–29.9 kg/m^2 was classified overweight, Participants with BMI≥30.0 kg/m^2 were considered obese (WHO, 2000).

3.7.3 Specimen collection and biochemical analysis

Blood samples were collected from 100 type 2 diabetic patients. Fasting overnight venous blood sample (about 5 ml) were drawn by the researcher himself into vacutainer plane tubes from all individuals. The blood was left for two tubes, first with anticoagulant and second without anticoagulant to allow blood to clot. Then, serum samples were obtained by centrifugation at room temperature at 4000 rpm/10 minutes. Serum glucose, urea, creatinine, cholesterol,

triglycerides, HDL-C, LDL-C, AST, and ALT were analyzed and whole blood with anticoagulant used to measured HbA1c.

3.8 Calculated measurements

- **Low density lipoprotein** was calculated by Friedewald equation:

  LDL (mg/dl) = cholesterol – (HDL + triglycerides/5))

3.9 Materials

3.9.1 Chemicals and reagents

Chemicals and reagents used in this study are shown in the following Table:

Reagent	Supplier
Glucose	Diasys Diagnostic Systems, Germany
HbA1c	Diasys Diagnostic Systems, Germany
Urea	Diasys Diagnostic Systems, Germany
Creatinine	Diasys Diagnostic Systems, Germany
Cholesterol	Diasys Diagnostic Systems, Germany
Uric Acid	Diasys Diagnostic Systems, Germany
Triglycerides	Diasys Diagnostic Systems, Germany
HDL-C	Diasys Diagnostic Systems, Germany
AST	Diasys Diagnostic Systems, Germany
ALT	Diasys Diagnostic Systems, Germany

3.9.2 Equipment

The main equipment that was used are listed in the following Table:

Instrument	Manufacturer
Spectrophotometer	Stat Fax-1904 Plus, Awareness Technology Inc. USA
Centrifuge	Elektro-mag, Turkey
Refrigerator with Freezer -20C	LG, Korea
Water Bath	Julabo, Germany
Vortex Mixer	Elektro-mag, Turkey
Micropipettes	Eppendorf, Germany
Balance	CAMRY, China
Meter	Measuring 3m/10ft, China

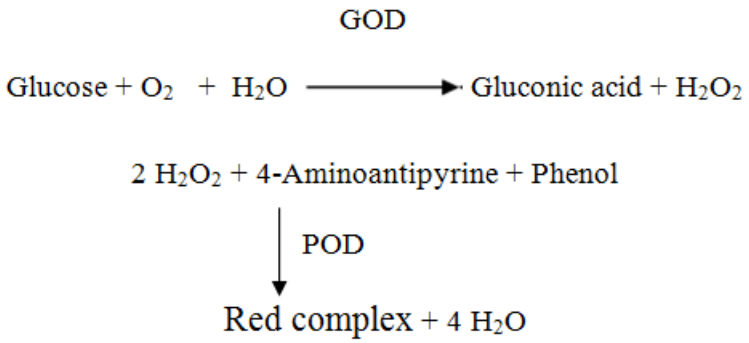
3.10 Biochemical analysis

3.10.1 Quantitative determination of fasting serum glucose (FPG)

Glucose concentration was determined according to the method originally described by Trinder, (1969).

Principle:

Glucose is converted by glucose oxidase (GOD) into hydrogen peroxide and gluconic acid, in presence of peroxidase (POD) were reacts with phenol and 4-amino antipyrine to form a red complex, whose intensity at 505 nm is proportional to the glucose concentration in the sample.



Reagent composition:

Active ingredients	Concentration
Glucose Reagent:	
Phosphate buffer pH 7.4	25 g/l
Phenol	< 0.9 g/l
4-Aminoantipirine	0.4 mmol/l
Glucose oxidase (GOD)	≥ 30 kU/l
Peroxidase (POD)	≥ 1 kU/l
Standard Glucose:	100 mg/dl

Assay procedure:

1) One ml of the ready to use reagent was pipetted into the bottom of three 2.5 ml glass tubes labeled as Sample, Standard, and Blank.
2) A volume of 0.01 ml serum sample, Glucose Standard, and deionized water was added to the Sample, Standard and Blank glass tubes, respectively.

3) The mixtures in the three glass tubes were mixed by pipetting up and down.
4) The mixtures in the three glass tubes were incubated at 37 ºC for 10 minutes.
5) The absorbance of the Sample and Standard was measured against Blank at 505 nm.

Calculations:

$$\text{Glucose concentration (mg/dL)} = \frac{\text{Absorbance of Sample}}{\text{Absorbance of Standard}} \text{ X } \text{Standard concentration value}$$

3.10.2 Quantitative determination of glycohemoglobin (HbA1C)

HbA1C concentration in whole blood was determined using an optimized ion-exchange resin procedure previously described by (Trivelli, Ranney, & Lai 1971).

Principle:

Mix A preparation of hemolyzed whole blood with a weakly binding cation-exchange resin. The HbA0 (non-glycosylated hemoglobin) bound to the resin, leaving free HbA1 to remove by means of a resin separator in the supernatant. The HbA1percent is assess by measuring the absorbance values at 415 nm of the HbA1 fraction and of the total Hb fraction, calculating the ratio of absorbance values, and comparing this ratio to that of a glycohemoglobin standard carried through the same procedure. Results are express as HbA1, but can be converted or derived as HbA1c by using a conversion factor (conversion factor = 13) or when using HbA1c value for the standard.

Reagent composition:

Active ingredients	Concentration
Glycohemoglobin ion exchange resin	Each tube contains 3 ml cation - exchange resin 8 mg/dl. pH 6.
Glycohemoglobin lysing reagent	It contains potassium cyanide 10 mmol/L and surfactants
Glycohemoglobin Standard (Lyophilized)	Prepared from packed human erythrocytes

Assay procedure:

Glycohemoglobin assay

1) A volume of 500 µl of the Glycohemoglobin lysing reagent was pipetted into the bottom of three 2.5 ml glass tubes labelled as Unknown (U), Standard (S) and Control (C).
2) A volume of 0.1 ml of a well-mixed whole blood sample, Glycohemoglobin Standard, and Glycohemoglobin Control was added to the unknown (U), Standard (S) and Control (C) glass tubes, respectively.
3) The mixtures in the three glass tubes were mixed by pipetting up and down and allowed to stand for 5 minutes at room temperature.
4) Three Glycohemoglobin ion exchange resin tubes were labelled as Unknown (U), Standard (S) and Control (C).
5) A volume of 0.1 ml of the prepared hemolysate was pipetted into the corresponding resin tubes.
6) A resin separator was positioned in the resin tube so the rubber sleeve is approximately 1-2 cm above the liquid level.
7) The resin tubes were mixed on a hematology rocker for 5 minutes, and then the resin separator was pushed into the tube until the resin is firmly packed in the bottom of the tube.
8) Each supernatant was poured directly into a separate cuvette and the absorbance ($A_{Glycohemoglobin}$) of the unknown (U), Standard (S) and Control (C) was measured against deionized water at 415 nm.

Total hemoglobin assay

1) A volume of 5 ml of deionized water was pipetted into the bottom of three 2.5 ml glass tubes labeled as Unknown (U), Standard (S) and Control (C).
2) A volume of 0.02 ml of the prepared hemolysate was pipetted into the corresponding glass tubes.
3) The mixtures in the three glass tubes were mixed by pipetting up and down and the absorbance (T_{total}) of the unknown (U), Standard (S) and Control (C) was measured against deionized water at 415 nm.

Calculations:

For each Unknown (U) and Standard (S), the ratio (R) of the glycohemoglobin absorbance ($A_{Glycohemoglobin}$) to the total hemoglobin absorbance (A_{Total}) was calculated as follows:

$$\text{Ratio (R) of the absorbance} = \frac{A_{Glycohemoglobin}}{A_{Total}}$$

$$\text{Hemoglobin (\%)} = \frac{\text{(R) of the Unknown (U)}}{\text{(R) of the Standard (S)}} \text{ X } \text{Hemoglobin Standard (\%)}$$

Results may also be reported as HbA1c when compared to the reference A1C method, the Stanbio method showed a 98% correlation with an equation of:

$$Y \text{ (A1c value)} = 0.838 \text{ x (Stanbio value)} - 0.732$$

The value obtained by the Stanbio method may be converted to calculated A1c value by use of this formula. For a direct calculated A1c value, the value of the Standard may be changed to 7.6% in lieu of the 10.0% and the results were A1c values.

3.10.3 Determination of serum urea

Urea was assessed by using "Urease-GLDH": enzymatic UV test, according to Thomas method (Wahlefeld, Wahlefeld, & Bergmeyer, 1974) using DiaSys reagent kits.

Principle

$$\text{Urea} + 2H_2O \xrightarrow{\text{Urease}} 2NH_4 + 2HCO$$

$$\text{2-Oxoglutarate} + NH_4 + NADH \xrightarrow{GLDH} \text{L-Glutamate} + NAD^+ + H_2O$$

Reagents

Concentrations are those in the final test mixture.

Reagent	Concentration
R1: TRIS	120 mmol/l
2- Oxoglutarate	7 mmol/l
ADP	0.6 mmol/l
Urease	≥ 0.6 ku/l
GLDH	≥ 1 ku/l
R2: NADH	0.25 mmol/l
Standard	50 mg/dl

Assay procedure

The working solution was prepared by mixing 4 parts of R1 with 1 part of R2.

Wavelength: 340 nm

Optical path: 1cm

Temperature: 37 ºC

Measurement: against distilled water.

- 10 µl of standard (sample or control) was added to 1 ml of working reagent and mixed well.
- The mixture was incubated for 30 sec then absorbance (A1) was recorded.
- After exactly further 60 sec the absorbance (A2) was measured.

Calculation

$\Delta A = (A1 - A2)$ sample or standard

$$\text{Urea [mg/dl]} = \frac{\Delta A \text{ sample X concentration of standard}}{\Delta A \text{ standard}}$$

Reference value (PCLTG, 2005)

Child	5 - 30 mg/dl
Adult	13 - 45 mg/dl

3.10.4 Quantitative determination of creatinine (Cr)

Creatinine concentration was determined according to the method originally described by **Fabiny and Ertingshausen, (1971)**.

Principle:

Serum and urine creatinine reacts with picric acid in alkaline solution yielding a yellow-orange colored compound. The intensity of the color is directly proportional to the creatinine concentration present in the sample.

$$\text{Creatinine + Picric acid} \xrightarrow{\text{Sodium hydroxide}} \text{Creatinine picrate complex}$$

Reagent composition:

Active ingredients	Concentration
Reagent A:	
Sodium hydroxide	1.25 mmol/l
Reagent B:	
Picric acid	20.5 mmol/l
Standard Creatinine:	2 mg/dl

One part of Reagent A and one part of Reagent B were mixed to obtain the working reagent.

Assay procedure:

1) One ml of the working reagent was pipetted into the bottom of three 2.5 ml glass tubes labeled as Sample, Standard, and Blank.
2) A volume of 0.1 ml sample (serum or 1:25 diluted urine), Creatinine Standard and deionized water was added to the Sample, Standard, and Blank glass tubes, respectively.
3) The mixtures in the three glass tubes were mixed by pipetting up and down and the absorbance (A1) of the Sample and Standard was measured against Blank at 490-510 nm after 10 seconds.
4) The absorbance (A2) of the Sample and Standard was measured again after 1 minute.
5) ΔA (A2−A1) for the Sample and Standard was calculated.

Calculations:

$$\text{Serum creatinine concentration (mg/dL)} = \frac{\Delta A \text{ of Sample}}{\Delta A \text{ of Standard}} \times \text{Standard concentration value}$$

3.10.5 Quantitative determination of uric acid (UA)

Uric acid concentration was determined according to the method originally described by **Fossati, Prencipe & Berti, (1980)**

Principle:

Uric acid is oxidized by uricase into allantoin with the production of hydrogen peroxide which, under the catalytic influence of peroxidase (POD), reacts with ESPT to form a blue-violet color:

$$\text{Uric acid} + O_2 + 2\,H_2O \xrightarrow{\text{Uricase}} \text{Allantoin} + CO_2 + H_2O_2$$

$$2\,H_2O_2 + \text{4-Aminoantipyrine} + \text{ESPT} \xrightarrow{\text{POD}} \text{Indamine} + 3\,H_2O$$

The color intensity, measured at 550 nm, is proportional to the uric acid present in the sample.

Reagent composition:

Active ingredients	Concentration
Uric acid Reagent:	
Borate Buffer pH 7.0	180 mmol/l
Uricase	> 50 U/l
Cholesterol esterase (CHE)	> 300 U/l
4-aminophenazone	0.25 mmol/l
ESPT	1 mmol/l
Peroxidase (POD)	> 100 U/l
Standard Uric acid:	6 mg/dl

Assay procedure:

1) One ml of the ready to use reagent was pipetted into the bottom of three 2.5 ml glass tubes labeled as Sample, Standard, and Blank.
2) A volume of 0.025 ml serum sample, Uric acid Standard, and deionized water was added to the Sample, Standard, and Blank glass tubes, respectively.
3) The mixtures in the three glass tubes were mixed by pipetting up and down.
4) The mixtures in the three glass tubes were incubated at room temperature for 15 minutes.
5) The absorbance of the Sample and Standard was measured against Blank at 550 nm.

Calculations:

$$\text{Uric acid concentration (mg/dL)} = \frac{\text{Absorbance of Sample}}{\text{Absorbance of Standard}} \text{ X } \text{Standard concentration value}$$

3.10.6 Quantitative determination total cholesterol (TC)

Total cholesterol concentration was determined according to the method originally described by **Meiattini et al., (1978)**.

Principle:

Cholesterol ester is hydrolyzed by cholesterol esterase (CHE) into fatty acids and cholesterol, which is oxidized in presence of cholesterol oxidase (CHO) into cholest-4-en-3-one and hydrogen peroxide, which reacts with phenol and 4-aminoantipirine in presence of POD to form a red complex, whose intensity at 505 nm is proportional to the cholesterol concentration in the sample.

$$\text{Cholesterol ester} + H_2O \xrightarrow{\text{CHE}} \text{cholesterol} + \text{fatty acids}$$

$$\text{Cholesterol} + O_2 \xrightarrow{\text{CHO}} \text{Cholest-4-en-3-one} + H_2O_2$$

$$2\,H_2O_2 + \text{4-Aminoantipyrine} + \text{Phenol} \xrightarrow{\text{POD}} \text{red complex} + 4\,H_2O$$

Reagent composition:

Active ingredients	Concentration
Cholesterol Reagent:	
Good's buffer (pH 6.7)	50 mmol/l
Phenol	5 mmol/l
4- Aminoantipyrine	0.3 mmol/l
Cholesterol esterase (CHE)	≥ 300 U/l
Cholesterol oxidase (CHO)	≥ 100 U/l
Peroxidase (POD)	≥ 500 U/l
Standard Cholesterol:	200 mg/dl

Assay procedure:

1) One ml of the ready to use reagent was pipetted into the bottom of three 2.5 ml glass tubes labelled as Sample, Standard, and Blank.
2) A volume of 0.01 ml serum sample, Cholesterol Standard, and deionized water was added to the Sample, Standard, and Blank glass tubes, respectively.
3) The mixtures in the three glass tubes were mixed by pipetting up and down.
4) The mixtures in the three glass tubes were incubated at 37 ºC for 10 minutes.
5) The absorbance of the Sample and Standard was measured against Blank at 510 nm.

Calculations:

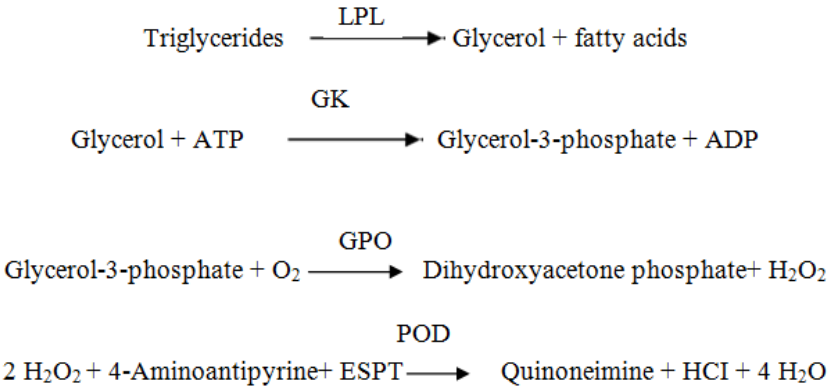
$$\text{Cholesterol concentration (mg/dL)} = \frac{\text{Absorbance of Sample}}{\text{Absorbance of Standard}} \text{ X } \text{Standard concentration value}$$

3.10.7 Quantitative determination triglycerides (TG)

Triglycerides concentration was determined according to the method originally described by **Bucolo and David, (1973).**

Principle:

Glycerol, released from triglycerides after hydrolysis with lipoprotein lipase (LPL), is transformed by glycerol kinase (GK) into glycerol-3-phosphate which is oxidized by glycerol phosphate oxidase (GPO) into dihydroxyacetone phosphate and hydrogen peroxide. In presence of peroxidase and 4-amino antipyrine, the hydrogen peroxide oxidizes the chromogen N-ethyl-N-(hydroxy-3-sulphopropil)-p-toluidine (ESPT) to form purple quinoneimine whose color intensity, measured at 550 nm, is proportional to the concentration of triglycerides in the sample.



Reagent composition:

Active ingredients	**Concentration**
Triglycerides Reagent:	
Good's buffer (pH 7.2)	50 mmol/l
ESPT	4 mmol/l
ATP	2 mmol/l
Mg^{++}	2 mmol/l
Lipoprotein lipase (LPL)	≥ 1 KU/I
Glycerol kinase (GK)	≥ 0.4 KU/I
Glycerol-3-phosphate-oxidase (GPO)	≥ 1.5 KU/I
Peroxidase (POD)	> 1 KU/I
4-Aminoantipyrine	0.5 mmol/l
Standard Glycerol:	200 mg/dl

Assay procedure:

1) One ml of the ready to use reagent was pipetted into the bottom of three 2.5 ml glass tubes labeled as Sample, Standard, and Blank.
2) A volume of 0.01 ml serum sample, Triglycerides Standard, and deionized water was added to the Sample, Standard and Blank glass tubes, respectively.
3) The mixtures in the three glass tubes were mixed by pipetting up and down.

4) The mixtures in the three glass tubes were incubated at 37 ºC for 10 minutes.
5) The absorbance of the Sample and Standard was measured against Blank at 550 nm.

Calculations:

$$\text{Triglycerides concentration (mg/dL)} = \frac{\text{Absorbance of Sample}}{\text{Absorbance of Standard}} \text{ X } \text{Standard concentration value}$$

3.10.8 Quantitative determination high-density lipoprotein cholesterol (HDL-C)

High-density lipoprotein cholesterol concentration was determined according to the method originally described by **Grove, (1979).**

Principle:

Chylomicrons, VLDL and LDL are precipitated by phosphotungstic acid and magnesium ions present in the precipitating reagent. Subsequent centrifugation leaves only the HDL-C in the supernatant, their cholesterol content is determined using the cholesterol reagent.

Reagent composition:

Active ingredients	Concentration
Precipitating Reagent:	
Magnesium chloride	1.4 mmol/l
Phosphotungstic acid	8.6 mmol/l
Cholesterol Reagent:	
Good's buffer (pH 6.7)	50 mmol/l
Phenol	5 mmol/l
4- Aminoantipyrine	0.3 mmol/l
Cholesterol esterase (CHE)	≥ 300 U/l
Cholesterol oxidase (CHO)	≥ 100 U/l
Peroxidase (POD)	≥ 500 U/l
Standard Cholesterol:	200 mg/dl

Assay procedure:

1) A volume of 200 µl of sample was added to 500 µl of the precipitation reagent and mixed well.
2) The mixture was allowed to stand for 15 minute at room temperature, and then centrifuged for 20 minutes at 4000 rpm.
3) One ml of the ready to use reagent was pipetted into the bottom of three 2.5 ml glass tubes labeled as Sample, Standard, and Blank.
4) A volume of 0.1 ml supernatant, Cholesterol Standard, and deionized water was added to the Sample, Standard, and Blank glass tubes, respectively.
5) The mixtures in the three glass tubes were mixed by pipetting up and down.
6) The mixtures in the three glass tubes were incubated at 37 ºC for 5 minutes.
7) The absorbance of the Sample and Standard was measured against Blank at 510 nm.

Calculations:

$$\text{HDL-C concentration (mg/dL)} = \frac{\text{Absorbance of Sample}}{\text{Absorbance of Standard}} \text{ X } \text{Standard concentration value}$$

3.10.9 Quantitative determination of serum low-density lipoproteins cholesterol (LDL-C)

Low-density lipoprotein cholesterol (LDL-C) levels were calculated using the formula of **Friedewald, Levy & Fredrickson, (1972).**

$$\text{LDL-C} = \text{Total Cholesterol} - (\text{HDL-C} + \text{triglycerides} / 5)$$

3.10.10 Determination of serum Aspartate aminotransferase (AST) enzyme activity

Serum aspartate aminotransferase activity was measured by using optimized UV test according to the international federation of clinical chemistry and laboratory medicine (Thomas 1998), using Diasys reagent Kits.

Principle

The principle of the method is based on the following enzymatic reactions:

$$\text{L-Aspartate} + \text{2-Oxoglutarate} \xrightarrow{\text{AST}} \text{L-Glutammate} + \text{Oxalacetate}$$

$$\text{Oxalacetate} + \text{NADH} + \text{H+} \xrightarrow{\text{MDH}} \text{L-Malate} + \text{NAD+}$$

The decrease in absorbance value at 340 nm, due to the oxidation of NADH to NAD+, is directly proportional to the AST activity in the sample.

The composition of reagents.

Reagent	Concentration
Reagent A:	
TRIS	28 mmol/l
EDTA-Na2	5.68 mmol/l
L-Aspartate	284 mmol/l
MDH	≥ 800 U/l
Sodium azide	2 g /l
Reagent B:	
2-Oxoglutarato	68 mmol/l
NADH	1.12 mmol/l
Sodium azide	0.095 g/l

preparation of reagents

Bireagent procedure. The reagents are liquids ready to use.

Monoreagent procedure. Ten parts of Reagent A and one part of Reagent B to obtain the working reagent (ex. 20 ml of RA + 2 ml of RB).

Analytical procedure

About 0.5 ml of serum was transferred to the chemistry auto analyzer to perform the test according to these parameters:

Parameter	**Value**
Reagent (µl)	200
Serum (µl)	20
Incubation period (s)	15 cycle(3.5minutes)
Reaction type	Kinetic
Wavelength (nm)	340
Reaction	Descending

Calculation

From absorbance reading calculates ΔA /min was calculated and multiply by the corresponding factor:

ΔA /min X factor (1745) = AST activity [U/l]

Reference value

Male:	10-50 U/l
Female:	10-35 U/l

3.10.11 Determination of alanine aminotransferase (ALT)

Serum alanine aminotransferase (ALT) activity was measured by using optimized UV-test according to International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), according to Guder method **Guder, Narayanan , Wisser & Zawta, (2001)** using DiaSys reagent kits.

Principle

L-Alanine + 2-Oxoglutarate $\xrightarrow{ALT}$ L-Glutamate + Pyruvate

Pyruvate + NADH + H+ $\xrightarrow{LDH}$ D-Lactate + NAD+

Components	Concentration
Reagent 1	
TRIS pH 7.15	140 mmol/l
L-Alanine	700 mmol/l
LDH (Lactate dehydrogenase)	≥ 2300 U/l
Reagent 2	
2-Oxoglutarate	85 mmol/l
NADH	1 mmol/l

Preparation of reagents

Bireagent procedure. The reagents are liquids ready to use.

Monoreagent procedure. Ten parts of Reagent A and one part of Reagent B to obtain the working reagent (ex. 20 ml of RA + 2 ml of RB).

Analytical procedure

About 0.5 ml of serum was transferred to the chemistry auto analyzer to perform the test according to these parameters:

Parameter	Value
Reagent (µI)	200
Serum (µI)	20
Incubation period (s)	15 cycle(3.5minutes)
Reaction type	Kinetic
Wavelength (nm)	340
Reaction	Descending

Calculation

From absorbance reading calculates ΔA /min and multiply by the corresponding factor:

ΔA /min X factor (1745) = ALT activity [U/l]

Reference value

Male:	10-50 U/l
Female:	10-35 U/l

3.11 Data analysis

Data were analyzed using Statistical Package for Social Sciences (SPSS) system version 23. The following statistical tests were applied:

- Frequency distributions
- Chi – Square Test
- Independent-samples t-test
- Pearson's correlation test

The percentage difference was calculated according to the formula:

$$\text{Percentage difference} = \frac{(\text{mean of patient} - \text{mean of control}) \times 100}{(\text{mean of patient} + \text{mean of control})/2}$$

Probability values (P) were obtained from the student's table of 't' and significance was at $P < 0.05$.

The range of minimum and maximum values were used. Graphs were plotted using SPSS system version 23.

Chapter 4

Results

Chapter 4

Results

4.1 Personal profile and life style of the study population.

Table (4.1) summarizes personal profile and life style of the study population. The study included 100 cases (50 males and 50 females). The study population included 36 (36%) good controls and 64 (64%) poor controls. On the other hands, the good control was included 12 (33.3%) males and 24 (66.7%) females. In contrast, poor control included 38 (59.4%) males and 26 (40.6%) females. the age was group (40-60) years old, the total mean age of study populations were 50.7±5.6 years. Good and poor control age was 48.4 ± 6.4 and 52 ± 4.7 years, respectively. The independent sample t-test showed a significant difference between means age of good and poor control (t= -3.25, P = 0.002). Analysis of the educational status of the study population showed that 12 (33.3%) good control and 4 (6.3%) poor control had finished university degree , 18 (50%) good and 12 (18.8%) had finished secondary school,5 (13.9%) and 30 (46.9%) had finished preparatory school , 0 (0%) and 14 (21.9%) had passed primary school , and 1 (2.8%) and 4 (6.3%) were illiterate for good and poor, respectively. The difference between various educational levels of good and poor controls was statistically significant (χ^2= 33.656, P = 0.001). Three (8.3%) of good control compared to 17 (26.6%) of were smokers among good and poor, respectively. the statistical test illustrated there was an association between smoking and poor controls (χ^2= 4.785, P = 0.029). Additionally, The number of good control who have physical activity 18 (50%) was significantly higher than poor cases (χ^2= 5.563, P = 0.018).

Table (4.1): Personal profile and life style of the study population

Variables	Total (n=100)	T2DM		Statistical test	P-value
		Good control (n=36)	Poor control (n=64)		
Age ±SD(years) (Min - max)	50.7±5.6 (40-60)	48.4±6.4 (40-60)	52±4.7 (40-60)	t = -3.253	0.002
Gender n (%) Male Female	 50 (50) 50 (50)	 12 (33.3) 24 (66.7)	 38 (59.4) 26 (40.6)	χ^2 = 6.25	0.012
Education n (%) University Secondary school Preparatory school Primary school Illiterate	 16 (16) 30 (30) 35 (35) 14 (14) 5 (5)	 12 (33.3) 18 (50) 5 (13.9) 0 (0) 1 (2.8)	 4 (6.3) 12 (18.8) 30 (46.9) 14 (21.9) 4 (6.3)	χ^2= 33.656	<0.001
Smoking n (%) Yes No	 20 (20) 80 (80)	 3 (8.3) 33 (91.7)	 17 (26.6) 47 (73.4)	χ^2= 4.785	0.029
Physical activity n (%) Yes No	 35 (35) 65 (65)	 18 (50) 18 (50)	 17 (26.6) 47 (73.4)	χ^2= 5.563	0.018

T2DM: type 2 diabetes mellitus; **n:** number; **χ^2:**chi square test, **t:** student t test. P < 0.05: significant, P ≥ 0.05: not significant

4.2 Economic characters of the study population

Economic characters of the study population are provided in table 4.2. The employed were 10 (27.8%) and 4 (6.3%) among good and poor control respectively. On the others hand, 26 (72.2%) good and 60 (93.8%) poor controls were unemployed respectively. the statistical test showed the positive relation between employers and good controls (χ^2=8.869, P = 0.003). In addition, Family income (month) also showed statistically significant difference between good and poor controls (χ^2 = 17.172, P< 0.001)

Table (4.2): Economic characteristics of the study population

Variables	Total (n=100)	T2DM		Statistical test	
		Good control (n=36)	Poor control (n=64)	χ^2	P-value
Employment n (%)					
Yes	14 (14)	10 (27.8)	4 (6.3)	8.869	0.003
No	86 (86)	26 (72.2)	60 (93.8)		
Family income (NIS/ month) n (%)					
<1000	59 (59)	12 (33.3)	47 (73.4)	17.172	<0.001
1000-2000	32 (32)	17 (47.2)	15 (23.4)		
>2000	9 (9)	7 (19.4)	2 (3.1)		

T2DM: type 2 diabetes mellitus, **n:** number, χ^2**:**chi square test, P < 0.05: significant, P ≥ 0.05: not significant

4.3 Anthropometric measurements of the study population

Table 4.3 shows the anthropometric measurements of the study population. The mean weight of good controls were lower significant than poor controls (84.4± 14.8 vs 96.2 ± 15.4 kg, respectively, % difference =13.1, t=-3.725 and P = 0.001). In contrast, there was no significant difference in the mean height of good compared to poor control (166± 9.9 % vs 166.3 ± 9.8 cm, respectively, % difference = 0.2 , t = -0.159 and P = 0.874). Therefore, increase body mass index (BMI) were associated with poor controls compare to good controls (35± 6 .0 vs 30.6±5.0, %difference = 13.3, t = -3.698 and P = 0.001).

Table (4.3): Anthropometric measurements of the study population

Variables	Total (n=100)	T2DM		Statistical test		
		Good control (n=36)	Poor control (n=64)	% difference	t	P-value
Weight (kg/m^2) Mean ± SD (Min - max)	91.9±16.2 (50-154)	84.4±14.8 (50-125)	96.2±15.4 (61-154)	13.1	-3.725	<0.001
Height (cm) Mean ± SD (Min - max)	166.2±9.8 (142-194)	166±9.9 (142-181)	166.3±9.8 (148-194)	0.2	-0.159	0.874
BMI (kg/m^2) Mean ± SD (Min - max)	33.4±6.0 (21.6-49.7)	30.6±5.0 (21.6-44.3)	35±6.0 (21.8-49.7)	13.3	-3.698	<0.001

T2DM: type 2 diabetes mellitus, **SD:**standard deviation **n:** number, **t:** student t test, $P < 0.05$: significant, $P \geq 0.05$: not significant

4.4 Clinical data of the study population.

The clinical data of the study population is pointed in table 4.4. The means duration of disease of good control was 4.6 ± 1.2 compared to poor control 4.5± 1.2 years, the t test showed no statistical significant between good and poor controls (t =0.432, P = 0.667). The compliance of medical of good control was 35(97.2%) and poor control was 58(90.6%). the chi square test was shown there was no statically significant between good and poor controls (χ^2 = 1.540, P = 0.215). regarding family history, there was 16 (44.4%) of good control and 48 (75%) poor controls have a family history of DM. Also, There was statistically significant between good and poor control for having family history of DM (χ^2 = 9.336, P = 0.002). On the other hand, no significant association between who had regular blood glucose monitoring (χ^2 = 0.037, P = 0.848) and the patient was taken Glucophage &doanil drugs (χ^2 = 0.174, P = 0.667) among good and poor controls.

Table (4.4): Clinical data of the study population.

Variables	Total (n=100)	T2DM		Statistical test	P-value
		Good control (n=36)	Poor control (n=64)		
Duration(years) Mean ± SD (Min – max)	4.5±5.7 (3-6)	4.6±1.2 (3-6)	4.5±1.2 (3-6)	t = 0.432	0.667
Compliance of medication n (%) Yes No	93 (93) 7 (7)	35 (97.2) 1 (2.8)	58 (90.6) 6 (9.4)	χ^2= 1.540	0.215
Family history of DM n (%) Yes No	64 (64) 36 (36)	16 (44.4) 20 (55.6)	48 (75) 16 (25)	χ^2= 9.336	0.002
Regular blood glucose monitoring n (%) **Yes** **No**	95 (95) 5 (5)	34 (94.4) 2 (5.6)	61 (95.3) 3 (4.7)	χ^2= 0.037	0.848
If yeas Daily Weekly Monthly	93(93) 5 (5) 2 (2)	34 (94.4) 2 (5.6) 0 (0)	59 (92.2) 3 (4.7) 2 (3.1)	χ^2= 1.172	0.556
Glucophage & Doanil n (%) Yes No	98 (98) 2 (2)	35 (97.2) 1 (2.8)	63 (98.4) 1 (1.6)	χ^2= 0.174	0.677

T2DM: type 2 diabetes mellitus, **SD:**standard deviation **n:** number, χ^2**:**chi square test, **t:** student t test, P < 0.05: significant, P ≥ 0.05: not significant**.**

4.5 T2DM complications among the study population

The T2DM complications among the study population are summarized in Table (4.5). The percentages of cardiovascular and retinopathy disease were significantly higher in poor control compared to good control (20.3 and 31.3% versus 2.8 and 8.3%, χ^2= 5.884, P = 0.15 and χ^2 = 6.832, P = 0.009, respectively). Similar the percentages neuropathy and nephropathy disease were significantly higher in poor control compared to good control (21.9 and 21.9 % versus o and 2.8%, χ^2=9.157, P = 0.002 and χ^2=6.590, P = 0.010, respectively).

Table (4.5): T2DM complications among the study population

Complications	Total (n=100)	T2DM		Statistical test	
		Good control (n=36)	Poor control (n=64)	χ^2	P-value
CVD n (%) Yes No	14 (14) 86 (86)	1 (2.8) 35 (97.2)	13 (20.3) 51 (79.7)	5.884	0.015
Retinopathy n (%) Yes No	23 (23) 77 (77)	3 (8.3) 33 (91.7)	20 (31.3) 44 (68.8)	6.832	0.009
Neuropathy n (%) Yes No	14 (14) 86 (86)	0 (0) 36 (100)	14 (21.9) 50 (78.1)	9.157	0.002
Nephropathy n (%) Yes No	15 (15) 85 (85)	1 (2.8) 35 (97.2)	14 (21.9) 50 (78.1)	6.590	0.010

T2DM: type 2 diabetes mellitus, **CVD:** Cardiovascular diseases, **n:** number, **χ^2:**chi square test, P < 0.05: significant, P ≥ 0.05: not significant

4.6 Food intake of the study population

Table (4.6) Summarized food intake of the study population. The chi square test shown there was statistically significant different between poor and good controls for bean (4(6.3%), 15(23.4), 45(70.3%) vs10(27.8 %) 7(19.4%), 19(52.8 %), (χ^2 = 8.901 , P = 0.012) and candy 28(43.8%), 12(18.8%) and 24(37.5%) vs 26(72.2 %), 7(19.4%) and 3(8.4%); χ^2 = 10.714, P = 0.005) among one time, time and ≥3 time, respectively. In contrast, there was no statistically significantly different between poor and good controls for who eating meat, fish, fruits, vegetables, dairy and its derivatives, dairy and its derivatives, cereals, olive oil compared to who not had it (P≥0.05).

Table (4.6): food intake of the study population

Food intake/week	Total (n=100)	T2DM		Statistical test	
		Good control (n=36)	Poor control (n=64)	χ^2	P-value
Bean n (%)					
One Time	14 (14)	10 (27.8)	4 (6.3)	8.901	0.012
Two Time	22 (22)	7 (19.4)	15 (23.4)		
≥3	64 (64)	19 (52.8)	45 (70.3)		
Candy n (%)					
One Time	54 (54)	26 (72.2)	28 (43.8)	10.724	0.005
Two Time	19 (19)	7 (19.4)	12 (18.8)		
≥ 3	27 (27)	3 (8.3)	24 (37.5)		
Meat n (%)					
One Time	49 (49)	18 (50)	31 (48.4)	4.212	0.122
Two Time	33 (33)	15 (41.7)	18 (28.1)		
≥3	18 (18)	3 (8.3)	15 (23.4)		
Fish n (%)					
One Time	89 (89)	33 (91.7)	56 (87.5)	1.053	0.591
Two Time	5 (5)	2 (5.6)	3 (4.7)		
≥3	6 (6)	1 (2.8)	5 (7.8)		
Fruits n (%)					
One Time	9 (9)	5 (13.9)	4 (6.3)	2.929	0.231
Two Time	7 (7)	1 (2.8)	6 (9.4)		
≥3	84 (84)	30 (83.3)	54 (84.4)		
Vegetable n (%)					
One Time	2 (2)	1 (2.8)	1 (1.6)	0.381	0.826
Two Time	4 (4)	1 (2.8)	3 (4.7)		
≥3	94 (94)	34 (94.4)	60 (93.8)		

Dairy And its Derivatives n (%)					
One Time	14 (14)	4 (11.1)	10 (15.6)	0.762	0.683
Two Time	11 (11)	5 (13.9)	6 (9.4)		
≥3	75 (75)	27 (75)	48 (75)		
Cereals n (%)					
One Time	56 (56)	22 (61.1)	34 (53.1)	0.757	0.685
Two Time	24 (24)	7 (19.4)	17 (26.6)		
≥3	20 (20)	7 (19.4)	13 (20.3)		
Olive Oil n (%)					
One Time	16 (16)	3 (8.3)	13 (20.3)	2.775	0.250
Two Time	13 (13)	6 (16.7)	7 (10.9)		
≥3	71 (71)	27 (75)	44 (68.8)		

T2DM: type 2 diabetes mellitus, **n:** number, χ^2**:**chi square test, P < 0.05: significant, P ≥ 0.05: not significant

4.7 Serum glucose, HBA1c, urea, creatinine & uric acid of the Study population

Serum glucose, HBAIC and kidney functions of the study population as indicated in table (4.7). The level of glucose among patient with poor controls was higher statistically significant than good controls (205.3±57.5 vs 106.0±20.6,% difference=63.8, t=-9.992, P<0.001). Also, the level of HbA1c among patient with poor controls was higher statistically significant than good controls (9.8±1.4 vs 6.2±0.8, % difference=45.8, t=-14.015, P<0.001). In addition, the levels of kidney function test were higher statistically significant in poor controls compared to good controls (urea was 35.4±11.2 vs 29.8±6, % difference=17.3%, t=-2.797, P = 0.006; creatinine was 1.0±0.3 vs 0.9±0.1,% difference=15.5%, t=-2.876, P = 0.005& uric acid was 4.4±1.1 vs 3.6±0.9,% difference=21%, t=-3.985, P<0.001, respectively).

Table (4.7): Serum glucose, HbA1c & kidney function of the Study population

Variables	Total (n=100)	T2DM		Statistical test		
		Good control (n=36)	Poor control (n=64)	% difference	t	P-value
Glucose (mg/dl) Mean ± SD (Min - max)	169.6±67.4 (78-318)	106.0±20.6 (78-180)	205.3±57.5 (102-318)	63.8	-9.992	<0.001
HbA1c (%) Mean ± SD (Min - max)	8.5±2.2 (3-13)	6.2±0.8 (3-7)	9.8±1.4 (7-13)	45.8	-14.015	<0.001
Urea (mg/dl) Mean ± SD (Min - max)	33.4±10 (21-85)	29.8±6 (22-45)	35.4±11.2 (21-85)	17.3	-2.797	0.006
Creatinine (mg/dl) Mean ± SD (Min - max)	1.0±0.3 (0.7-1.9)	0.9±0.1 (0.7-1.4)	1.0±0.3 (0.7-1.9)	15.5	-2.876	0.005
Uric acid (mg/dl) Mean ± SD (Min - max)	4.1±1.1 (2.7-9.7)	3.6±0.9 (2.9-6.9)	4.4±1.1 (2.7-9.7)	21.0	-3.985	<0.001

T2DM: type 2 diabetes mellitus, **HbA1c:** Hemoglobin A1c, **SD:**standard deviation **n:** number, **t:** student t test, $P < 0.05$: significant, $P \geq 0.05$: not significant

4.8 Lipid profile of the study population

Serum lipid profile including cholesterol, triglycerides, high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL – C) of the study population is illustrated in table (4.8). The average levels of cholesterol , triglycerides and LDL-C were higher statistically significant in poor control (212.1 ± 42.7, 203±111.4 and 129.7 ± 42.6 mg/dl, respectively) compared to good control (186.7 ±24.4, 154.4 ±66.6 and 107.1 ±25.9 mg/dl, respectively) with % differences of 12.8, 27.5 and 19.1 % & t = - 3.281, & P = 0.001 , t= - 2.412 & P = 0.018 and t= - 2.891& P = 0.005, respectively. In contrast, HDL – C was lower statistically significant in Poor compared to good controls (47.2 ± 4.3 vs 49.5 ± 2.4 mg/ dl, respectively, % difference = - 4.9, t = 3.075, P = 0.003).

Table (4.8): Lipid profile of the Study population

Variables	Total (n=100)	T2DM		Statistical test		
		Good control (n=36)	Poor control (n=64)	% difference	t	P-value
Cholesterol (mg/dl) Mean ± SD (Min - max)	203.0±39.0 (98-290)	186.7±24.4 (144-270)	212.1±42.7 (98-290)	12.8	-3.281	0.001
T.G (mg/dl) Mean ± SD (Min - max)	185.7±100 (73-588)	154.4±66.6 (73-390)	203.6±111.4 (74-588)	27.5	-2.412	0.018
HDL-C(mg/dl) Mean ± SD (Min - max)	48.0±3.9 (38-54)	49.5±2.4 (42-54)	47.2±4.3 (38-54)	-4.9	3.075	0.003
LDL-C(mg/dl) Mean ± SD (Min - max)	121.4±38.8 (70-218)	107.1±25.9 (70-204)	129.7±42.6 (70-218)	19.1	-2.891	0.005

T2DM: type 2 diabetes mellitus, **TG:** Triglyceride, **HDL-C:** High density lipoprotein cholesterol, **LDL-C:** Low density lipoprotein cholesterol, **SD:**standard deviation **n:** number, **t:** student t test, $P < 0.05$: significant, $P \geq 0.05$: not significant

4.9 liver function of the study population

The activities of serum ALT and AST as a marker of liver function are pointed out in table 4.9. There was statistical significant elevation in ALT and AST in poor control compared to good control (27.2 ± 12 and 28.9 ± 14.5 vs 21.6 ± 5.8 and 19.8 ± 68 u/L ,% difference 22.8 and 37.5 and P = 0.010 and 0.001, respectively).

Table (4.9): Liver function of the Study population

Variables	Total (n=100)	T2DM		Statistical test		
		Good control (n=36)	Poor control (n=64)	% difference	t	P-value
ALT(IU/L) Mean ± SD (Min - max)	25.2±10.5 (13-73)	21.6±5.8 (14-38)	27.2±12 (13-73)	22.8	-2.618	0.010
AST(IU/L) Mean ± SD (Min - max)	25.6±13.0 (13-80)	19.8±6.8 (13-51)	28.9±14.5 (13-80)	37.5	-3.551	0.001

ALT: alanine aminotransferase, **AST**: aspartate aminotransferase, **SD:**standard deviation **n:** number, **t:** student t test, $P < 0.05$: significant, $P \geq 0.05$: not significant

HbA1c in relation to studied parameters

Table (4.10) provides the relationships of HbA1c with Parameters of the study population. Results showed that the positive significant correlation between HbA1C and glucose, triglyceride and AST (r = 0.777, P = 0.001, Figure 4.1; r = 0.356; P = 0.001, Figure 4.2; and r = 0.225; P = 0.024, Figure 4.3, respective. On the other hand, there is a negative significant correlation between HbA1c and uric acid (r = -0.346 P = 0.001, Figure 4.4). Clearly, HbA1c were no significant correlation with age, duration, weight, height, BMI, cholesterols, HDL-C, LDL-C, ALT, urea and creatinine (P≥0.05).

Table (4.10): HbA1c in relation to studied parameters.

Parameters	**HbA1c** (%)	
	r	**P-value**
Age (years)	-0.119	0.236
Duration(years)	0.050	0.623
Weight (kg/m^2)	0.056	0.577
Height (cm)	-0.045	0.657
BMI (kg/m^2)	-0.059	0.559
Glucose (mg/dl)	0.777	<0.001*
Cholesterols (mg/dl)	0.125	0.217
T.G (mg/dl)	0.356	<0.001*
HDL-C (mg/dl)	-0.143	0.157
LDL-C (mg/dl)	0.091	0.370
AST (IU/L)	0.225	0.024 *
ALT (IU/L)	0.189	0.060
Urea (mg/dl)	-0.131	0.194
Creatinine (mg/dl)	-0.067	0.510
Uric acid (mg/dl)	-0.346	<0.001*

BMI: Body Mass Index, **HbA1c:** Hemoglobin A1c**, TG:** Triglyceride, **HDL-C:** High density lipoprotein cholesterol, **LDL-C:** Low density lipoprotein cholesterol, **ALT**: alanine aminotransferase, **AST**: aspartate aminotransferase. The correlation **(r)** was analyzed using Pearson correlation coefficient (normally distributed data). P < 0.05: significant, P ≥ 0.05: not significant

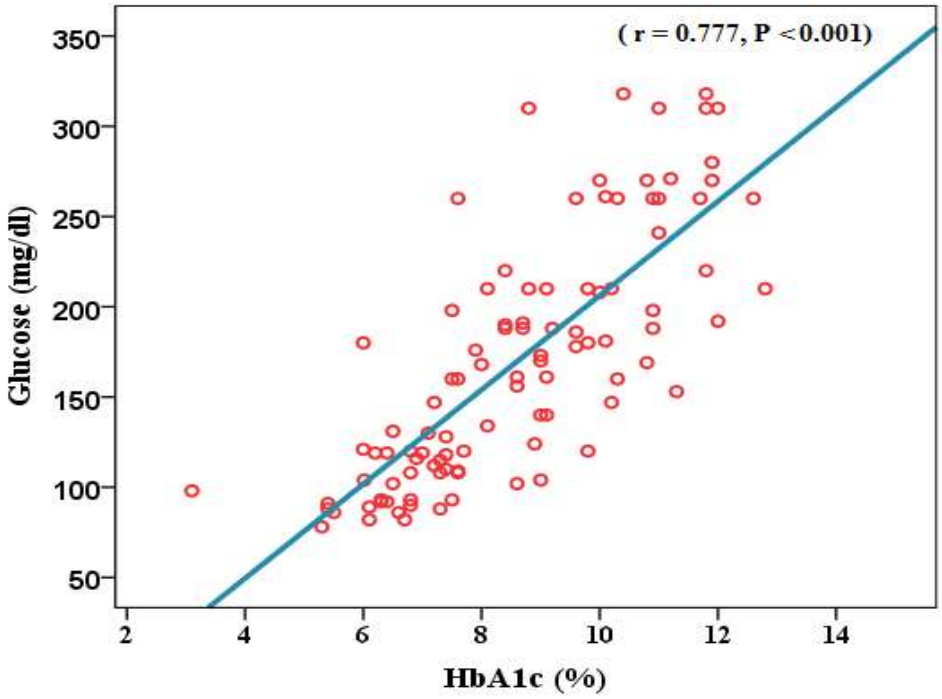


Figure (4.1): The positive correlation between HbA1cand glucose.

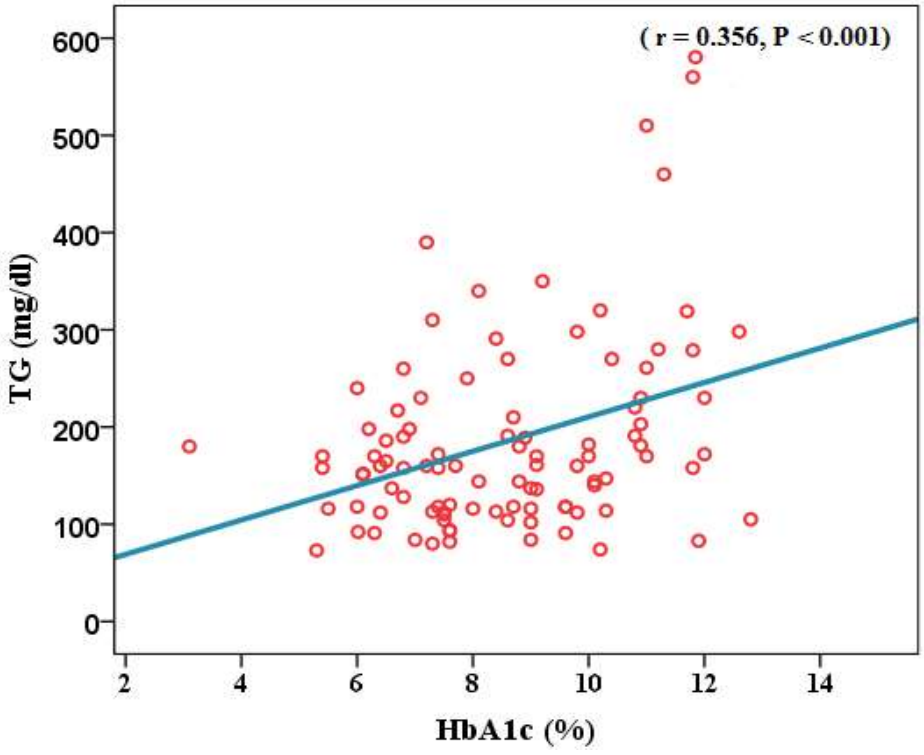


Figure (4.2): The positive correlation between HbA1cand TG.

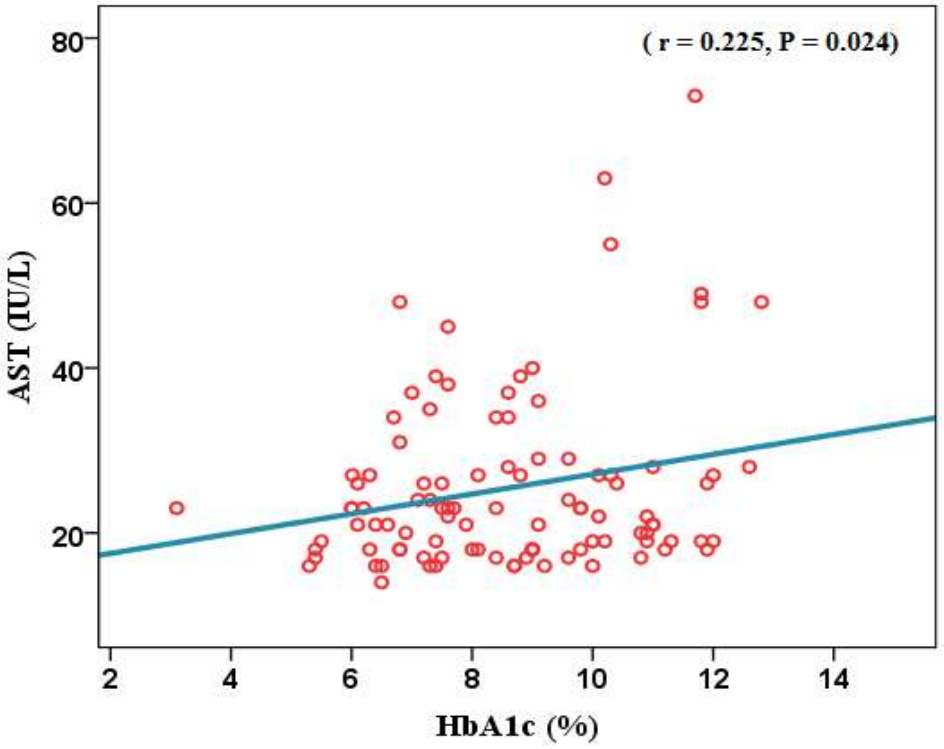


Figure (4.3): The positive correlation between HbA1cand AST.

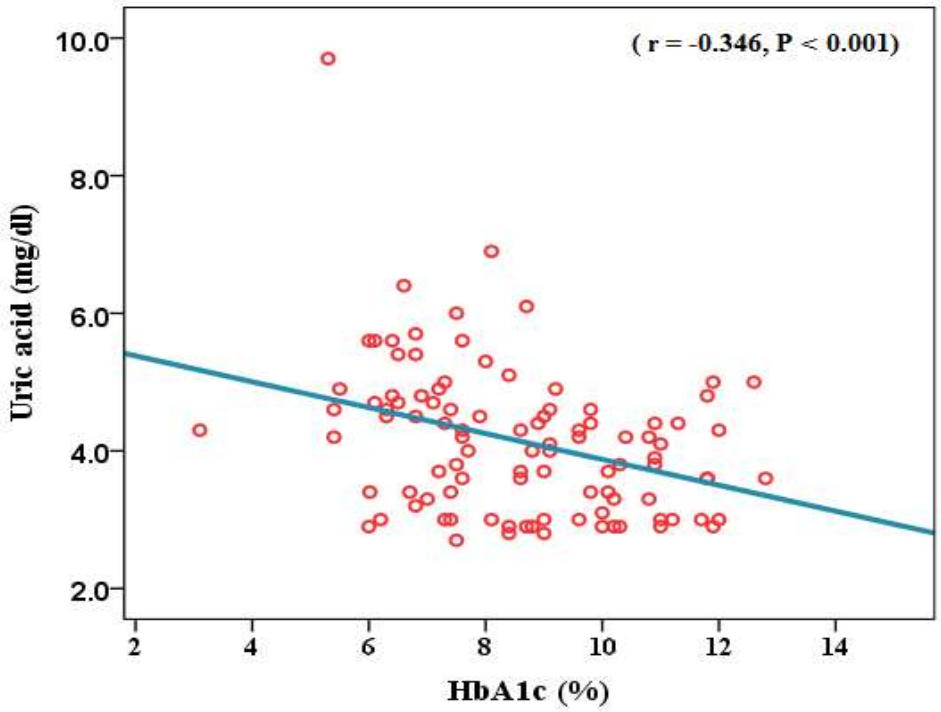


Figure (4.4): The negative correlation between HbA1cand uric acid.

4.10 Glucose in relation to studied parameter

Glucose in relation to studied parameters of the study population is pointed out in table (4.11). Results showed that the positive significant correlation between glucose and HbA1c (r = 0.777, P = 0.001, Figure 4.1); glucose and triglyceride (r = 0.297, P = 0.003, Figure 4.5). On the other hand, there is a negative significant correlation between glucose and uric acid (-0.330, P = 0.001, Figure 4.4). On the other hand, Glucose was no significant correlation age, duration, weight, height, BMI, cholesterols, HDL-C, LDL-C, AST, ALT, urea, and creatinine (P≥0.05).

Table (4.11): Glucose in relation to studied parameters

Parameters	**Glucose**(mg/dl)	
	r	**P-value**
Age (years)	-0.051	0.613
Duration(years)	0.019	0.853
Weight (kg/m^2)	-0.054	0.593
Height±SD(cm)	-0.152	0.131
BMI (kg/m^2)	-0.097	0.339
HbA1c (%)	0.777	<0.001*
Cholesterols (mg/dl)	0.163	0.106
T.G (mg/dl)	0.297	0.003*
HDL (mg/dl)	-0.164	0.103
LDL-C (mg/dl)	0.099	0.327
AST (IU/L)	0.100	0.324
ALT (IU/L)	0.065	0.520
Urea (mg/dl)	-0.119	0.240
Creatinine (mg/dl)	-0.025	0.807
Uric acid (mg/dl)	-0.330	0.001*

BMI: Body Mass Index, **HbA1c:** Hemoglobin A1c**, TG:** Triglyceride, **HDL-C:** High density lipoprotein cholesterol, **LDL-C:** Low density lipoprotein cholesterol, **ALT**: alanine aminotransferase, **AST**: aspartate aminotransferase. The correlation **(r)** was analyzed using Pearson correlation coefficient (normally distributed data). P < 0.05: significant, P ≥ 0.05: not significant.

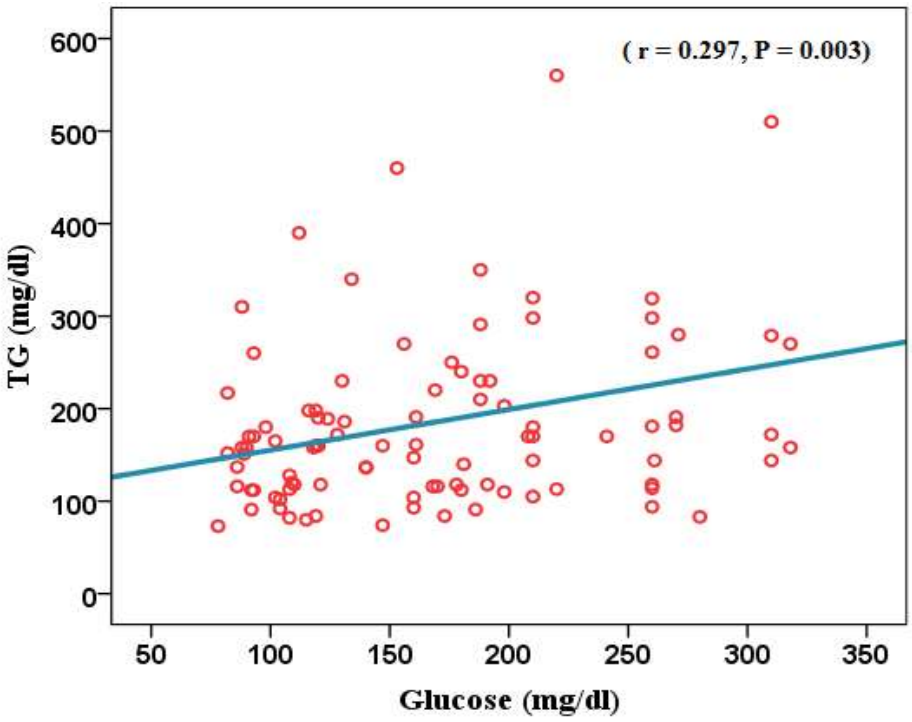


Figure (4.5): The positive correlation between Glucose and TG

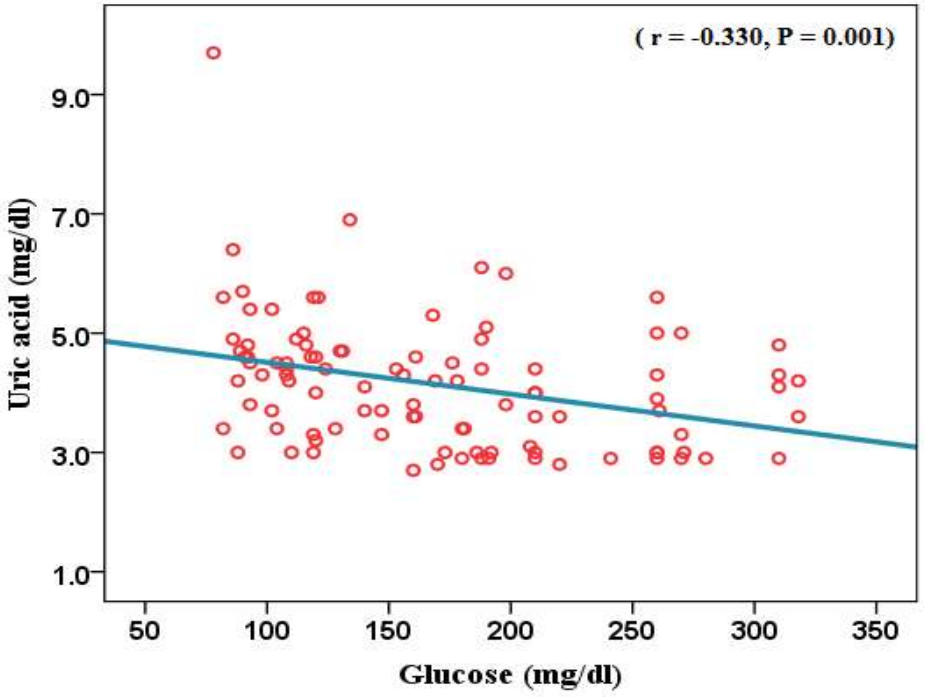


Figure (4.6): The negative correlation between glucose and uric acid

4.12: BMI in relation to studied parameters

BMI in relation to studied parameters is pointed in Table (4.12). The Pearson correlation showed positive significant correlation for BMI with height(r = 0.786, P = 0.001) and uric acid (r = 0.293, P = 000). In contrast, there for negative significant correlation between B.M.I and weight (r = -0.361, P = 0.001).

Table (4.12): BMI in relation to studied parameters

Parameters	BMI (kg/m^2)	
	r	P-value
Age (years)	0.018	0.857
Duration(years)	-0.092	0.365
Weight (kg/m^2)	-0.361	<0.001
Height± SD (cm)	0.786	<0.001
Glucose(mg/dl)	-0.097	0.339
HbA1c(%)	-0.059	0.559
Cholesterols(mg/dl)	-0.146	0.146
T.G(mg/dl)	-0.073	0.474
HDL–C (mg/dl)	0.097	0.339
LDL-C (mg/dl)	-0.137	0.176
AST(IU/L)	0.027	0.791
ALT(IU/L)	0.107	0.291
Urea(mg/dl)	-0.054	0.594
Creatinine(mg/dl)	-0.082	0.418
Uric acid(mg/dl)	0.293	0.003

BMI: Body Mass Index, **HbA1c:** Hemoglobin A1c**, TG:** Triglyceride, **HDL-C:** High density lipoprotein cholesterol, **LDL-C:** Low density lipoprotein cholesterol, **ALT**: alanine aminotransferase, **AST**: aspartate aminotransferase. The correlation **(r)** was analyzed using Pearson correlation coefficient (normally distributed data). $P < 0.05$: significant, $P \geq 0.05$: not significant

Chapter 5

Discussion

Chapter 5

Discussion

Diabetes mellitus (DM) is a rapidly growing public health problem that affects millions of people worldwide leading to disastrous consequences. DM is responsible for three forth of morbidity and 88% of mortality mostly in developing countries (International Diabetes Federation, 2015; Mathers & Loncar, 2006). In Palestine, the prevalence of DM reached 9% of the general population in which T2DM is the most prevalent type (> 87% of the cases) (Ministry of Health, MOH, 2006). The ultimate outcome of diabetes management is to achieve a glycemic control and to prevent or delay complications related to diabetes. In this study, we assessed the glycemic level, determined by HbA1c, and factors associated with good glycemic control among patients with T2DM.

The usefulness of program diet for T2DM patients has not been fully investigated in Gaza Governorate. Although few studies were have been assessed the clinical and dietary status of T2DM in Gaza Governorate (AbuMustafa and Yassin, 2017; Elsous, Radwan, Al-Sharif& & Mustafa, 2017; El Bilbeisi, Hosseini& Djafarian, 2017). Therefore, the present study is the first to demonstrate the relationship between dietary status and controls of T2DM and compared the effectiveness and safety of diet with good and poor controls by using HbA1c. In this cross sectional study, the prevalence of poor controls among T2DM were 64% and 36% were good controls, On the other hands, poor control included 59.4% males and 40.6% females. Data presented here suggested that more than half of T2DM patients have poor controls and male more than poor controls than females. Such finding is in agreement with that reported by Holden et al., (2017) and Tuligenga et al., (2014) and they showed increased likelihood of concomitant T2DM and worse diabetic control in patients with T2DM especially in men. This necessitates a lot of programs to

improve awareness T2DM patients for complications dangerous in cases uncontrolled glucose level and programs about disease management.

5.1 Personal profile and life style of the study population.

The total mean age of study populations were 50.7±5.6 years. As indicated in the present study, Poor control among T2DM patient had higher statistically significant of age (52 ± 4.7 years) than good controls (48.4 ± 6.4 years). Similar results were found by Ahmad, Islahudin, & Paraidathathu (2014); Terzin et al., (2014) and Masumoto et al., (2017).

Analysis of the educational status of the study population showed that 33.3% good control and 6.3% poor control had finished university degree , 50% good and 18.8% had finished secondary school, 13.9% and 46.9% had finished preparatory school , 0% and 21.9% had passed primary school , and 2.8% and 6.3% were illiterate for good and poor, respectively. Our results indicate poor controls among T2DM patients were significant associated with low education levels which agree with others reported (Camara et al., 2015 and Eborall et al., 2016).

The present study demonstrated shown an association between smoking and poor controls among T2DM patients, (26.6% vs 8.3% among poor and good, respectively). Campus et al., (2005) and Çetin et al., (2014) reported that association between smoking and poor controls among T2DM patients and they concluded the smoking as a risk factor among poor controls T2DM patients. Additionally, others studied suggested smoking effects on HbA1c levels and the requirement of hypoglycemic treatment in type 2 diabetic patients (Eliasson et al., 2003& Xu et al., (2014). In contrast, McCulloch et al., (2002) were reported that smoking does not have a significant direct effect in HbA1c in patients with type 2 diabetes mellitus.

The number of good control who have physical activity (50%) was significantly higher than poor cases (26.6%). This indicates Increase in physical activity is associated with lower HbA1c levels that decrease in complications among

T2DM patients. This study was in line with that of Chen et al., (2015) which concluded physical activity plays a very useful role in type 2 diabetes for induce muscles to use stored glucose (glycogen), as well as using glucose that is available in the blood, as fuel.

5.2 Economic characters of the study population

Economic characters of our study population were associated with poor controls. The numbers employed were lower among poor control (6.3%) than good control (27.8%). On the others hand, about three quarter (72.2%) of good and 93.8% poor controls were unemployed. the statistically positive significant relationship between economic levels and controls of blood HbA1c levels, In addition, Family income (NIS/ month) also showed statistically significant higher for good than poor controls. Many studied agree with our results for effect of economic levels on controls of HbA1c among T2DM patients and authors were suggested depression and stress among people with diabetes are play roles for elevated glucose levels (Steptoe et al., 2014 & Arora et al., 2016).

5.3 Anthropometric measurements of the study population

The present study demonstrated the mean weight of poor controls (96.2 ± 15.4 kg) were higher significant than good controls (84.4± 14.8). Similarly, increase body mass index (BMI) were significant associated with poor controls (35± 6 .0 kg/m^2) compare to good controls (30.6±5.0 kg/m^2). However, obese individuals are at elevated risk for diabetes. The literature suggested the present finding in that obesity is a high-risk factor for T2DM (Vidal et al., 2008, Cefalu et al., 2015). They reported that about more half of poor controls T2DM are obese. Chronic obesity leads to elevated insulin resistance that can be prognosis into diabetes, most likely because adipose tissue is a source of many chemical signals to tissues. Other research showed that poor controls of T2DM causes obesity by changes occur for metabolism and other deranged cell behavior attendant on insulin resistance (Tangvarasittichai et al., 2015 & Fu et al., 2017).

5.4 Clinical data of the study population.

On the light of the present results, the means of duration among poor control (4.5± 1.2 years) higher than good control (4.6 ± 1.2) but no statistically significant difference between good and poor controls for the duration. Our study does not agree with a lot of others studies that showed a positive significant correlation between HbA1c and duration of diabetic (Bode et al., 2015 and Raj & Rajan, 2017). These incompatible results may be due to new diagnostic cases among our study population with low range for the duration (3-6 years).

The compliance for antidiabetes agents that not only improve diabetic control but decrease or have a neutral effect on BMI with beneficial effects on lipids is ideal options for managing T2DM patients (Pi-Sunyer, 2009). The compliance of medical was 97.2% for good control and 90.6% for poor control with no statically significant between good and poor controls ($P \geq 0.05$). Medication adherence and associated HbA1c in type 2 diabetes were reported (Al-Qazaz et al., 2011 & Linetzky et al., 2017) that different with our result because of our study population new diagnostic and small sample size for good controls (36 cases only).

Regarding family history, statistically significant between good (44.4%) and poor control (75%) for have a family history ($P<0.05$). Also, on the other hand, no significant association between who had regular blood glucose monitoring and the patient taken Glucophage &doanil drugs among good and poor controls ($P \geq 0.05$). This result agrees with Meo et al., 2016 and Van Zon, Snieder, Bültmann, Reijneveld, (2017). They found significant association between family history of T2DM and poor controls. clearly, no association between who had regular blood glucose monitoring and the patient taken Glucophage & daniel drugs because of different source of medication among T2DM patients in Gaza Governorate (Governorate medical center, UN medical center, and commercial pharmacy).

5.5 The T2DM complications among the study population

The most self-reported symptoms among diabetic patients were cardiovascular, retinopathy, neuropathy, and nephropathy. The prevalence of such symptoms was positively associated with the poor progress of the disease i.e. the poor controls of diabetes mellitus, the higher the percentage of self-reported complications among patients than good controls ($P<0.05$). Several studies reported similar diabetic complications with increasing rates of disease progress among T2DM poor controls (Eskow & Oates, 2017 and Yin et al., 2016).

5.6 Food intake of the study population

Dietary are important modulators of glucose metabolism. However, few longitudinal studies have evaluated the associations between intake of protein and protein type and risk of T2DM (Malik et al., 2016). Clearly, there was statistically significantly difference between poor and good controls for bean and candy among one time, time and ≥3 time, respectively ($P<0.05$). In contrast, there was no statistically significant difference between poor and good controls for who eating meat, fish, fruits, vegetables, dairy and its derivatives, dairy and its derivatives, cereals, olive oil compared to who not had it ($P\geq0.05$). The majority of studies found a significant interrelationship between types of Food intake and poor controls.

Mohamed, Mustafa, Ibrahim & Åstrøm (2016) assess dietary habits, oral impact on daily performance and type 2 diabetes and they concluded oral impacts were more frequently reported in T2DM cases than controls. Independent of diabetic- and oral clinical status, dietary habits discriminated between individuals with and without oral impacts. The influence of meat and bread consumption on the oral impact on daily performance varied significantly according to T2DM status.

Cleary, Vitale et al., (2016) demonstrated that fluency of dietary fat and carbohydrates proportions on plasma lipids, glucose control and low-grade inflammation in patients with T2DM. They concluded people with T2DM, variations in the proportion of fat and carbohydrates in the diet, within the relatively narrow ranges recommended by different nutritional guidelines, significantly impact on the

metabolic profile. Also, they support the potential for reducing the intake of fat and added sugars, preferring complex, slowly absorbable, carbohydrates.

Glycemic control from 1988 to 2000 among u.s. adults diagnosed with type 2 diabetes was studied by Koro et al., (2004) and they showed treatment regimens among U.S. adults diagnosed with type 2 diabetes have changed substantially over the past 10 years. However, a decrease in glycemic control rates was also observed during this time period. This trend may contribute to increased rates of macrovascular and microvascular diabetic complications, which may impact health care costs. Our data support the public health message of implementation of early, aggressive management of diabetes.

5.7 Serum glucose, HbA1c & kidney function of the Study Population

The level of glucose, HbA1c, kidney function (urea, creatinine & uric acid) among patient with poor controls was higher statistically significant than good controls ($P<0.05$). The results suggested poor controls of T2DM associated with increased glucose levels that induce kidney impaired. This may be explained in part by the finding that many of diabetic patients did not compliance with diet regime. In addition, medication regime may be not followed. The high-fat diet was found to increase the risk of type 2 diabetes (Kemp et al., 2005).

In a previous study to assess non-compliance among 216 type 2 diabetic patients in Gaza Governorate, **Zakout, (2006)** reported that three-quarters of the study population had poor glycemic control and half of them were not compliance with the medication regimen. Typical reasons cited by patients included forgetfulness, frustration, feeling better without treatment, polypharmacy, fear from drug side-effect and unavailability of drugs.

As indicated in our data serum urea, creatinine and uric acid concentrations of diabetics associated increase among patient with poor controls compared to that of good controls. Urea is formed by the liver as an end product of protein breakdown and is one biomarker of the renal function and the uric acid is the end product of an exogenous pool of purines and endogenous purine metabolism (Saxena et al., 2017). Lowering in urea observed here may be

induce damage in its synthesis as a result of impaired liver function and due to defect in protein metabolism. Creatinine and uric acid are not clarified it from blood due to damage in real functions (Jalal et al., 2017).

Elevated serum creatinine and uric acid levels in poor controls diabetic patients may be related to disturbance of renal function (Wanner et al., 2016). In addition, the observed elevated in urea and creatinine and uric acid may be explained on the basis of increase glomerular filtration rate due to decrease creatinine clearing from blood by the kidney (Yassin & Altibi, 2011).

5.8 Lipid profile of the study population

Dyslipidemia with increased cholesterol, TG, and LDL-C concentration is common in T2DM patients (Mooradian et al., 2009). Our study showed an increase significant in the levels of total cholesterol, TG and LDL-C in poor controls when compared to good controls among T2DM patients. In contrast, there was a significant decrease in HDL-C level in diabetics. It was reported that cholesterol, TG, and LDL-C are an increase in poor controls of T2DM patients (Müller-Wieland et al., 2017, Rosso et al., 2017). The abnormal high concentrations of serum lipids profiles in T2DM is mainly elevated among the mobilization of free fatty acids from fat depots tissue, since insulin inhibits the hormone sensitive lipase. Excess lipids among poor controls T2DM are converted into TG, phospholipids, and cholesterol in hepatic cells. These three substances with amino acids may be discharged into circulation blood in the form of high and low density lipoproteins (Laverdy et al., 2016 and Fatani, Babakr, NourEldin, & Almarzouki, 2016).

5.9 liver function of the study population

The liver cells have multiple functions. It breaks down and distraction toxics substances in the human body. When the liver is damaged from disease or medication, liver enzymes as AST and ALT will be elevated and this enzymes widely used as sensitive and specific biomarkers when the liver is injured or damaged. In the present study, the activities liver marker such as ALT and AST are a statistically

significant elevated in poor control compared to good control. Elevations in markers of liver injury and risk of T2DM were reported (Lim et al., (2011). Our finding agrees with others studied by Harris et al., (2005) and reported individuals with poor controls of T2DM have a higher incidence of liver function test abnormalities than individuals who do good controls for T2DM. they suggested mild chronic elevations of AST and ALT enzymes often reflect underlying insulin resistance. Elevation of AST and ALT enzymes within three times the upper limits of normal is not a contraindication for starting oral antidiabetic or lipid-modifying therapy. In contrast, antidiabetic agents have generally been shown to decrease ALT levels as tighter blood glucose levels are achieved.

5.10 HbA1c in relation to studied parameters

On the light of the present results, HbA1c were had a positive significant correlation with glucose, TG, and AST. In contrast, there is a negative significant correlation between HbA1c and uric acid ($P<0.05$). On the other hand, HbA1c were no significant correlation with age, duration, weight, height, BMI, cholesterols, HDL-C, LDL-C, ALT, urea, and creatinine ($P>0.05$). This result agrees with Ketema & Kibret, 2015 and Khan, Sobki & Khan, (2007) they found HbA1c levels have a positive significant correlation with glucose, TG and AST. In contrast, Yuan et al., (2011) found a negative significant correlation between HbA1c and uric acid. There is much evidence supporting the statement that decreases in insulin secretion and glucose metabolism is the major mediators of poor controls among T2DM have poor controls (Takashi et al., 2017). Insulin level can stimulate the transcriptional activity of the glucose promoter among T2DM with poor controls (Fu et al., 2014).

5.11 Glucose and BMI in relation to studied parameter

Results illustrated the positive significant correlation between glucose and HbA1c; glucose and triglyceride. On the other hand, there is a negative significant correlation between HbA1c and uric acid ($P<0.05$). Clearly, Glucose no significant correlation between and age, duration, weight, height, BMI,

cholesterols, HDL-C, LDL-C, AST, ALT, urea, and creatinine (P>0.05). The Pearson correlation showed them positive significant correlation for BMI with height and uric acid. In contrast, there for negative significant correlation between BMI. Similar findings were reported by Hage, Lundman, Rydén, Mellbin (2013) and Arbel et al., (2014). Dyslipidemia may play a role in the presence of increased BMI that usually accompanied poor controls in T2DM (Cai et al., 2012).

Chapter 6

Conclusions and Recommendations

Chapter 6

Conclusions and Recommendations

6.1 Conclusions

1. The prevalence of poor controls (64%) were high among patients T2DM then good controls (36%). Regarding gender, males (59.4%) was more than female (40.6%) for poor controls of T2DM.
2. Decrease of education levels was significantly associated with poor controls among T2DM
3. Smoking was significantly associated with poor controls among T2DM patients
4. Increase physical activity was elevated among good control of T2DM.
5. The statistically positive significant relationship between economic levels and controls of blood HbA1c levels was observed. In addition, Family income also showed statistically significant association with good controls.
6. Body mass index (BMI) was significantly associated with poor controls compared to good controls.
7. The family history of T2DM was associated with poor control.
8. The self-reported symptoms among T2DM patients such as cardiovascular, retinopathy, neuropathy and nephropathy were strongly positively associated with the poor controls progress of T2DM.
9. Bean and candy intake were statistically associated with poor controls.
10. The level of glucose, HbA1c, kidney function (urea, creatinine & uric acid) among patient with poor controls was higher statistically significant than good controls
11. Elevated the levels of total cholesterol, TG, and LDL-C in poor controls when compared to good controls among T2DM patients.
12. Activities of liver marker such as ALT and AST are a statistically significant elevated in poor control compared to good control.

13. HbA1c was had a positive significant correlation with glucose, TG and AST. In contrast, there is a negative significant correlation between HbA1c and uric acid

6.2 Recommendations

1. Management of diabetes mellitus in term of diet and BMI is important to delay the development of diabetic complications.
2. Awareness, education programs, preventing smoking and increasing physical activity will improve good controls among T2DM that will lead to decrease self-reported symptoms among T2DM such as cardiovascular, retinopathy, neuropathy and nephropathy.
3. Decrease Bean and candy intake will be helpful for good controls for T2DM patients.
4. The controls of the level of glucose and HbA1c in diabetic patients could be helpful for preventing impaired kidney function.
5. Enhancement of T2DM patients to follow up lipid profiles, livers $ kidney function to manage diabetic complications.

References

References

AbuMustafa, A. A., & Yassin, M. (2017). Clinical and biochemical aspects associated with diabetic nephropathy among type 2 diabetic males in Gaza Governorate. *International Journal of Medicine*, *5*(1), 142-147.

Ahmad, N. S., Islahudin, F., & Paraidathathu, T. (2014). Factors associated with good glycemic control among patients with type 2 diabetes mellitus. *Journal of diabetes investigation*, *5*(5), 563-569.

Alebiosu, C.O., Ayodele, O.E. (2005): The global burden of chronic kidney disease and the way forward. *Ethnicity and Disease 15*(3), 418.

Al-Qazaz, H. K., Sulaiman, S. A., Hassali, M. A., Shafie, A. A., Sundram, S., Al-Nuri, R., & Saleem, F. (2011). Diabetes knowledge, medication adherence and glycemic control among patients with type 2 diabetes. *International journal of clinical pharmacy*, *33*(6), 1028-1035.

American Diabetes Association. (2014). Diagnosis and classification of diabetes mellitus. *Diabetes care*, *37*(Supplement 1), S81-S90.

American Diabetes Association. (2017). 2. Classification and diagnosis of diabetes. *Diabetes Care*, *40*(Supplement 1), S11-S24.

Arbel, Y., Zlotnik, M., Halkin, A., Havakuk, O., Berliner, S., Herz, I., ... & Banai, S. (2014). Admission glucose, fasting glucose, HbA1c levels and the SYNTAX score in non-diabetic patients undergoing coronary angiography. *Clinical Research in Cardiology*, *103*(3), 223-227.

Arora, M., Mahat, R. K., Kumar, S., Tyagi, S., & Batra, J. (2016). Oxidative stress and its relation to glycemic control in patients of type 2 diabetes mellitus. *International Journal of Medical Science and Public Health*, *5*(6), 1173-1177.

Astrup, A., Dyerberg, J., Elwood, P., Hermansen, K., Hu, F. B., Jakobsen, M. U., ... & Nestel, P. (2011). The role of reducing intakes of saturated fat in the prevention of cardiovascular disease: where does the evidence stand in 2010?. *The American journal of clinical nutrition*, *93*(4), 684-688.

Astrup, A.S., Tarnow, L., Rossing, P., Pietraszek, L., Riis ,Hansen, P., Parving, H.H. (2005): Improved prognosis in type 1 diabetic patients with nephropathy: a prospective follow-up study. *Kidney Int. 68*(3), 1250-1257.

Atiba, A. S., Oparinde, D. P., Babatunde, O. A., Niran-Atiba, T. A., Jimoh, A. K., & Adepeju, A. A. (2013). Liver enzymes and lipid profile among type 2 diabetic patients in Osogbo, Nigeria. *Greener Journal of Medical Sciences*, *3*(5), 174-8.

Bode, B., Stenlöf, K., Harris, S., Sullivan, D., Fung, A., Usiskin, K., & Meininger, G. (2015). Long-term efficacy and safety of canagliflozin over 104 weeks in patients aged 55–80 years with type 2 diabetes. *Diabetes, Obesity and Metabolism*, *17*(3), 294-303.

Bonner, C., Kerr-Conte, J., Gmyr, V., Queniat, G., Moerman, E., Thévenet, J., ... & Sener, A. (2015). Inhibition of the glucose transporter SGLT2 with dapagliflozin in pancreatic alpha cells triggers glucagon secretion. *Nature medicine*, *21*(5), 512-517.

Bucolo, G., & David, H. (1973). Quantitative determination of serum triglycerides by the use of enzymes. *Clinical chemistry*, *19*(5), 476-482.

Buyken, A. E., von Eckardstein, A., Schulte, H., Cullen, P., & Assmann, G. (2007). Type 2 diabetes mellitus and risk of coronary heart disease: results of the 10-year follow-up of the PROCAM study. *European Journal of Cardiovascular Prevention & Rehabilitation*, *14*(2), 230-236.

Cai, L., Zhang, L., Liu, A., Li, S., & Wang, P. (2012). Prevalence, awareness, treatment, and control of dyslipidemia among adults in Beijing, China. *Journal of atherosclerosis and thrombosis*, *19*(2), 159-168.

Camara, A., Baldé, N. M., Sobngwi-Tambekou, J., Kengne, A. P., Diallo, M. M., Tchatchoua, A. P., ... & Sobngwi, E. (2015). Poor glycemic control in type 2 diabetes in the South of the Sahara: The issue of limited access to an HbA1c test. *Diabetes research and clinical practice*, *108*(1), 187-192.

Campus, G., Salem, A., Uzzau, S., Baldoni, E., & Tonolo, G. (2005). Diabetes and periodontal disease: a case-control study. *Journal of periodontology*, *76*(3), 418-425.

Cefalu, W. T., Stenlöf, K., Leiter, L. A., Wilding, J. P., Blonde, L., Polidori, D., ... & Meininger, G. (2015). Effects of canagliflozin on body weight and relationship to HbA1c and blood pressure changes in patients with type 2 diabetes. *Diabetologia*, *58*(6), 1183-1187.

Çetin, S., Öztürk, M. A., Barındık, N., İmren, E., & Peker, Y. (2014). Increased coronary intervention rate among diabetic patients with poor glycaemic control: a cross-sectional study. *Bosnian journal of basic medical sciences*, *14*(1), 16.

Chandalia, M., Garg, A., Lutjohann, D., von Bergmann, K., Grundy, S. M., & Brinkley, L. J. (2000). Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. *New England Journal of Medicine*, *342*(19), 1392-1398.

Chandalia, M., Garg, A., Lutjohann, D., von Bergmann, K., Grundy, S. M., & Brinkley, L. J. (2000). Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. *New England Journal of Medicine*, *342*(19), 1392-1398.

Chapman, M. J., Ginsberg, H. N., Amarenco, P., Andreotti, F., Borén, J., Catapano, A. L., ... & Lesnik, P. (2011). Triglyceride-rich lipoproteins and high-density lipoprotein cholesterol in patients at high risk of cardiovascular disease: evidence and guidance for management. *European heart journal*, *32*(11), 1345-1361.

Chen, L., Pei, J. H., Kuang, J., Chen, H. M., Chen, Z., Li, Z. W., & Yang, H. Z. (2015). Effect of lifestyle intervention in patients with type 2 diabetes: a meta-analysis. *Metabolism*, *64*(2), 338-347.

Chen, M., Li, Y., Sun, Q., Pan, A., Manson, J. E., Rexrode, K. M., ... & Hu, F. B. (2016). Dairy fat and risk of cardiovascular disease in 3 cohorts of US adults. *The American journal of clinical nutrition*, *104*(5), 1209-1217.

Chin-Hong, P. V. (2006). Infections in patients with diabetes mellitus: importance of early recognition, treatment, and prevention. *Advanced Studies in Medicine*, *6*(2), 71.

Dall, T. M., Narayan, K. V., Gillespie, K. B., Gallo, P. D., Blanchard, T. D., Solcan, M., ... & Quick, W. W. (2014). Detecting type 2 diabetes and prediabetes among asymptomatic adults in the United States: modeling American Diabetes Association versus US Preventive Services Task Force diabetes screening guidelines. *Population health metrics*, *12*(1), 12.

Dash, S., Xiao, C., Stahel, P., Koulajian, K., Giacca, A., & Lewis, G. F. (2017). Evaluation of the specific effects of intranasal glucagon on circulating glucose and lipid concentrations in healthy males during a pancreatic clamp. *Diabetes, Obesity and Metabolism*.

DeFronzo, R. A., Tripathy, D., Schwenke, D. C., Banerji, M., Bray, G. A., Buchanan, T. A., ... & Mack, W. J. (2011). Pioglitazone for diabetes prevention in impaired glucose tolerance. *New England Journal of Medicine*, *364*(12), 1104-1115.

Den Besten, G., Bleeker, A., Gerding, A., van Eunen, K., Havinga, R., van Dijk, T. H., ... & Bakker, B. M. (2015). Short-chain fatty acids protect against high-fat diet–induced obesity via a PPARγ-dependent switch from lipogenesis to fat oxidation. *Diabetes*, *64*(7), 2398-2408.

Dhatariya, K. K., & Umpierrez, G. E. (2017). Guidelines for management of diabetic ketoacidosis: time to revise?. *The Lancet Diabetes & Endocrinology*, *5*(5), 321-323.

Eborall, H. C., Virdee, S. K., Patel, N., Redwood, S., Greenfield, S. M., & Stone, M. A. (2016). "And now for the good news…" the impact of negative and positive messages in self-management education for people with Type 2 diabetes: A qualitative study in an ethnically diverse population. *Chronic illness*, *12*(1), 3-17.

El Bilbeisi, A. H., Hosseini, S., & Djafarian, K. (2017). Dietary patterns and metabolic syndrome among type 2 diabetes patients in Gaza Governorate, Palestine. *Ethiopian Journal of Health Sciences*, *27*(3), 227-238.

Eliasson, B. (2003). Cigarette smoking and diabetes. *Progress in cardiovascular diseases*, *45*(5), 405-413.

Elsous, A., Radwan, M., Al-Sharif, H., & Mustafa, A. A. (2017). Medications adherence and associated Factors among Patients with Type 2 Diabetes Mellitus in the Gaza Governorate, Palestine. *Frontiers in Endocrinology*, *8*.

Engelgau, M. M., Thompson, T. J., Herman, W. H., Boyle, J. P., Aubert, R. E., Kenny, S. J., ... & Ali, M. A. (1997). Comparison of fasting and 2-hour glucose and HbA 1c levels for diagnosing diabetes: diagnostic criteria and performance revisited. *Diabetes care*, *20*(5), 785-791.

Eskow, C. C., & Oates, T. W. (2017). Dental Implant Survival and Complication Rate over 2 Years for Individuals with Poorly Controlled Type 2 Diabetes Mellitus. *Clinical implant dentistry and related research*, *19*(3), 423-431.

Fabiny, D. L., & Ertingshausen, G. (1971). Automated reaction-rate method for determination of serum creatinine with the CentrifiChem. *Clinical chemistry*, *17*(8), 696-700.

Farsani, S. F., Brodovicz, K., Soleymanlou, N., Marquard, J., Wissinger, E., & Maiese, B. A. (2017). Incidence and prevalence of diabetic ketoacidosis (DKA) among adults with type 1 diabetes mellitus (T1D): a systematic literature review. *BMJ open*, *7*(7), e016587.

Fatani, S. H., Babakr, A. T., NourEldin, E. M., & Almarzouki, A. A. (2016). Lipid peroxidation is associated with poor control of type-2 diabetes mellitus. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, *10*(2), S64-S67.

Fayfman, M., Pasquel, F. J., & Umpierrez, G. E. (2017). Management of Hyperglycemic Crises: Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar State. *Medical Clinics of North America*, *101*(3), 587-606.

Forbes, J. M., Soldatos, G., & Thomas, M. C. (2005). Below the Radar: Advanced Glycation End Products that Detour "around the side": Is HbA1c not an accurate enough predictor of long term progression and glycaemic control in diabetes?. *The Clinical biochemist. Reviews/Australian Association of Clinical Biochemists.*, *26*(4), 123.

Fossati, P., Prencipe, L., & Berti, G. (1980). Use of 3, 5-dichloro-2-hydroxybenzenesulfonic acid/4-aminophenazone chromogenic system in direct enzymic assay of uric acid in serum and urine. *Clinical chemistry*, *26*(2), 227-231.

Frank, N., & Tadros, E. M. (2014). Insulin dysregulation. *Equine veterinary journal*, *46*(1), 103-112.

Freeman, R. (2013). Diabetic autonomic neuropathy. *Handbook of clinical neurology*, *126*, 63-79.

Friedewald, W. T., Levy, R. I., & Fredrickson, D. S. (1972). Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical chemistry*, *18*(6), 499-502.

Fu, S., Lin, Y., Ping, P., Luo, L., & Ye, P. (2017). Overall obesity had similar ability to identify the insulin resistance and pancreatic β-cell function compared with abdominal obesity in Chinese community-dwelling population without type 2 diabetes. *INTERNATIONAL JOURNAL OF CLINICAL AND EXPERIMENTAL MEDICINE*, *10*(3), 5293-5299.

Fu, Z., Berhane, F., Fite, A., Seyoum, B., Abou-Samra, A. B., & Zhang, R. (2014). Elevated circulating lipasin/betatrophin in human type 2 diabetes and obesity. *Scientific reports*, *4*.

Grove, T. H. (1979). Effect of reagent pH on determination of high-density lipoprotein cholesterol by precipitation with sodium phosphotungstate-magnesium. *Clinical Chemistry*, *25*(4), 560-564.

Guder W.G., Narayanan S.,Wisser H. and Zawta B. (2001): The Quality of Diagnostic Samples. Brochure in: Samples: From the Patient to the Laboratory, 2nd edition. Darmstadt: GIT-Verlag.

Gutmann, I., Wahlefeld, A. W., & Bergmeyer, H. U. (1974). Methods of enzymatic analysis. *New York: Academic Press*, *3*, 1464.

Hage, C., Lundman, P., Rydén, L., & Mellbin, L. (2013). Fasting glucose, HbA1c, or oral glucose tolerance testing for the detection of glucose abnormalities in patients with acute coronary syndromes. *European journal of preventive cardiology*, *20*(4), 549-554.

Hammes, H.P., Lemmen, K.D., Bertram, B. (2014): Diabetic Retinopathy and Maculopathy. Experimental and clinical endocrinology & diabetes, *Exp Clin Endocrinol Diabetes. 122(7):* 387-390.

Harris, E. H. (2005). Elevated liver function tests in type 2 diabetes. *Clinical diabetes*, *23*(3), 115-119.

Holden, S. E., Jenkins-Jones, S., Morgan, C. L., Peters, J. R., Schernthaner, G., & Currie, C. J. (2017). Prevalence, glucose control and relative survival of people with Type 2 diabetes in the UK from 1991 to 2013. *Diabetic Medicine*, *34*(6), 770-780.

Husseini, A., Abu-Rmeileh, N. M., Mikki, N., Ramahi, T. M., Ghosh, H. A., Barghuthi, N., ... & Jervell, J. (2009). Cardiovascular diseases, diabetes mellitus, and cancer in the occupied Palestinian territory. *The lancet*, *373*(9668), 1041-1049.

International Diabetes Federation (IDF) (2015). Diabetes Atlas 7th ed. Available at: http://www.diabetesatlas.org/. accessed 02 Aug 2017

International Expert Committee. (2009). International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. *Diabetes care*, *32*(7), 1327-1334.

Jaikumkao, K., Pongchaidecha, A., Chatsudthipong, V., Chattipakorn, S. C., Chattipakorn, N., & Lungkaphin, A. (2017). The roles of sodium-glucose cotransporter 2 inhibitors in preventing kidney injury in diabetes. *Biomedicine & Pharmacotherapy*, *94*, 176-187.

Jalal, D.I., Decker, E., Perrenoud, L., Nowak, K.L., Bispham, N., Mehta, T., Smits, G., You, Z., Seals, D., Chonchol, M. and Johnson, R.J., 2017. Vascular function and uric acid-lowering in stage 3 CKD. Journal of the American Society of Nephrology, 28(3), pp.943-952.

Jannasch, F., Kröger, J., & Schulze, M. B. (2017). Dietary Patterns and Type 2 Diabetes: A Systematic Literature Review and Meta-Analysis of Prospective Studies. *The Journal of Nutrition*, *147*(6), 1174-1182.

Jochmann, C., & Hammes, H. P. (2002). Epidemiology, pathogenesis and therapy of diabetic retinopathy and maculopathy. *Zeitschrift fur arztliche Fortbildung und Qualitatssicherung*, *96*(3), 167-174.

Kamata, Y., Takano, K., Kishihara, E., Watanabe, M., Ichikawa, R., & Shichiri, M. (2017). Distinct clinical characteristics and therapeutic modalities for diabetic ketoacidosis in type 1 and type 2 diabetes mellitus. *Journal of diabetes and its complications*, *31*(2), 468-472.

Kanasaki, K., Taduri, G., Koya, D. (2013): Diabetic nephropathy: the role of inflammation in fibroblast activation and kidney fibrosis. Front Endocrinol (Lausanne) (6)4:7.

Kashiwagi, A., Kasuga, M., Araki, E., Oka, Y., Hanafusa, T., Ito, H., ... & Sanke, T. (2012). International clinical harmonization of glycated hemoglobin in Japan: from Japan Diabetes Society to National Glycohemoglobin Standardization Program values. *Journal of diabetes investigation*, *3*(1), 39-40.

Kaufman, F. R., Gallivan, J. M., & Warren-Boulton, E. (2009). Overview of diabetes in children and teens. *American Journal of Health Education*, *40*(5), 259-263.

Kemp, T. M., Barr, E. L., Zimmet, P. Z., Cameron, A. J., Welborn, T. A., Colagiuri, S., ... & Shaw, J. E. (2005). Glucose, lipid, and blood pressure control in Australian adults with type 2 diabetes. *Diabetes care*, *28*(6), 1490-1492.

Ketema, E. B., & Kibret, K. T. (2015). Correlation of fasting and postprandial plasma glucose with HbA1c in assessing glycemic control; systematic review and meta-analysis. *Archives of Public Health*, *73*(1), 43.

Khan, H. A., Sobki, S. H., & Khan, S. A. (2007). Association between glycaemic control and serum lipids profile in type 2 diabetic patients: HbA1c predicts dyslipidaemia. *Clinical and experimental medicine*, *7*(1), 24-29.

Khan, M., Iqbal Haider, S. N., Humayun, M., & Khan, A. (2016). An Atypical Presentation Of Hyperosmolar Non-Ketotic Coma. *Cell*, *312*, 597-5936.

Kollannoor-Samuel, G., Shebl, F. M., Hawley, N. L., & Pérez-Escamilla, R. (2016). Nutrition facts panel use is associated with higher diet quality and lower glycated hemoglobin concentrations in US adults with undiagnosed prediabetes. *The American journal of clinical nutrition*, *104*(6), 1639-1646.

Koro, C. E., Bowlin, S. J., Bourgeois, N., & Fedder, D. O. (2004). Glycemic control from 1988 to 2000 among US adults diagnosed with type 2 diabetes. *Diabetes care*, *27*(1), 17-20.

Landon, Mark B., Lisa Mele, Catherine Y. Spong, Marshall W. Carpenter, Susan M. Ramin, Brian Casey, Ronald J. Wapner et al. "The relationship between maternal glycemia and perinatal outcome." *Obstetrics and gynecology* 117, no. 2 0 1 (2011): 218.

Laverdy, O. G., Hueb, W. A., Sprandel, M. C. O., Kalil-Filho, R., & Maranhao, R. C.

(2015). Effects of glycemic control upon serum lipids and lipid transfers to HDL in patients with type 2 diabetes mellitus: novel findings in unesterified cholesterol status. *Experimental and Clinical Endocrinology & Diabetes*, *123*(04), 232-239.

Lewko, B., & Stepinski, J. (2009): Hyperglycemia and mechanical stress: targeting the renal podocyte. J Cell Physiol. 221(2): 288-295.

Ley, S. H., Hamdy, O., Mohan, V., & Hu, F. B. (2014). Prevention and management of type 2 diabetes: dietary components and nutritional strategies. *The Lancet*, *383*(9933), 1999-2007.

Lim, E. L., Hollingsworth, K. G., Aribisala, B. S., Chen, M. J., Mathers, J. C., & Taylor, R. (2011). Reversal of type 2 diabetes: normalisation of beta cell function in association with decreased pancreas and liver triacylglycerol. *Diabetologia*, *54*(10), 2506-2514.

Linetzky, B., Jiang, D., Funnell, M. M., Curtis, B. H., & Polonsky, W. H. (2017). Exploring the role of the patient–physician relationship on insulin adherence and clinical outcomes in type 2 diabetes: Insights from the MOSAIc study. *Journal of diabetes*, *9*(6), 596-605.

Malik, V. S., Li, Y., Tobias, D. K., Pan, A., & Hu, F. B. (2016). Dietary protein intake and risk of type 2 diabetes in US men and women. *American journal of epidemiology*, *183*(8), 715-728.

Masumoto, N., Otsuki, H., Iwakawa, S., Inada, S., & Koga, M. (2017). Usefulness of glycated albumin in decisions regarding the discontinuation of a diabetes drug and factors associated with poor glycemic control following discontinuation in patients with type 2 diabetes mellitus. *Diabetology International*, *8*(1), 39-44.

Mathers, CD., Loncar, D., (2006). Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med*;3:e442.

McCulloch, P., Lee, S., Higgins, R., McCall, K., & Schade, D. S. (2002). Effect of smoking on hemoglobin A1c and body mass index in patients with type 2 diabetes mellitus. *Journal of investigative medicine: the official publication of the American Federation for Clinical Research*, *50*(4), 284-287.

Meiattini, F., Prencipe, L., Bardelli, F., Giannini, G., & Tarli, P. (1978). The 4-hydroxybenzoate/4-aminophenazone chromogenic system used in the enzymic determination of serum cholesterol. *Clinical Chemistry*, *24*(12), 2161-2165.

Meo, S. A., Alsubaie, Y., Almubarak, Z., Almutawa, H., AlQasem, Y., & Hasanato, R. M. (2016). Response to Comments on Meo et al. Association of Exposure to Radio-Frequency Electromagnetic Field Radiation (RF-EMFR) Generated by Mobile Phone Base Stations with Glycated Hemoglobin (HbA1c) and Risk of Type 2 Diabetes Mellitus. Int. J. Environ. Res. Public Health, 2015, 12, 14519–14528. *International journal of environmental research and public health*, *13*(3), 262.

Meyer, K. A., Kushi, L. H., Jacobs, D. R., Slavin, J., Sellers, T. A., & Folsom, A. R. (2000). Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. *The American journal of clinical nutrition*, *71*(4), 921-930.

Micha, R., Peñalvo, J. L., Cudhea, F., Imamura, F., Rehm, C. D., & Mozaffarian, D. (2017). Association between dietary factors and mortality from heart disease, stroke, and type 2 diabetes in the United States. *Jama*, *317*(9), 912-924.

Ministry of Health (MOH) (2006). Health status in Palestine. Palestine, Gaza: Ministry of Health,

Mohamed, H. G., Mustafa, K., Ibrahim, S. O., & Åstrøm, A. N. (2017). Dietary habits, oral impact on daily performance and type 2 diabetes: a matched case-control study from Sudan. *Health and quality of life outcomes*, *15*(1), 111.

Møller, G., Sluik, D., Ritz, C., Mikkilä, V., Raitakari, O. T., Hutri-Kähönen, N., ... & Feskens, E. J. (2017). A Protein Diet Score, Including Plant and Animal Protein, Investigating the Association with HbA1c and eGFR—The PREVIEW Project. *Nutrients*, *9*(7), 763.

Mooradian, A. D. (2009). Dyslipidemia in type 2 diabetes mellitus. *Nature Reviews. Endocrinology*, *5*(3), 150.

Müller-Wieland, D., Leiter, L. A., Cariou, B., Letierce, A., Colhoun, H. M., Prato, S., ... & Ray, K. K. (2017). Design and rationale of the ODYSSEY DM-DYSLIPIDEMIA trial: lipid-lowering efficacy and safety of alirocumab in individuals with type 2 diabetes and mixed dyslipidaemia at high cardiovascular risk. *Cardiovascular diabetology*, *16*(1), 70.

Nakamura, M. T., Yudell, B. E., & Loor, J. J. (2014). Regulation of energy metabolism by long-chain fatty acids. *Progress in lipid research*, *53*, 124-144.

National Diabetes Data Group. (1979). Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes*, *28*(12), 1039-1057.

Nishihama, K., Maki, K., Okano, Y., Hashimoto, R., Hotta, Y., Uemura, M., ... & Yano, Y. (2017). A case of type 2 diabetes mellitus with metformin-associated lactic acidosis initially presenting the appearance of a sulfonylurea-related hypoglycemic attack. *Acute Medicine & Surgery*, *4*(1), 123-126.

Nishimura, R., Tanaka, Y., Koiwai, K., Inoue, K., Hach, T., Salsali, A., ... & Broedl, U. C. (2015). Effect of empagliflozin monotherapy on postprandial glucose and 24-hour glucose variability in Japanese patients with type 2 diabetes mellitus: a randomized, double-blind, placebo-controlled, 4-week study. *Cardiovascular diabetology*, *14*(1), 11.

Odegaard, J. I., & Chawla, A. (2013). Pleiotropic actions of insulin resistance and inflammation in metabolic homeostasis. *Science*, *339*(6116), 172-177.

Peng, J., Li, X., Zhang, D., Chen, J. K., Su, Y., Smith, S. B., & Dong, Z. (2015). Hyperglycemia, p53 and mitochondrial pathway of apoptosis are involved in the susceptibility of diabetic models to ischemic acute kidney injury. *Kidney international*, *87*(1), 137.

Peters, A. L., Buschur, E. O., Buse, J. B., Cohan, P., Diner, J. C., & Hirsch, I. B. (2015). Euglycemic diabetic ketoacidosis: a potential complication of treatment with sodium–glucose cotransporter 2 inhibition. *Diabetes care*, *38*(9), 1687-1693.

Pi-Sunyer, F. X. (2009). The impact of weight gain on motivation, compliance, and metabolic control in patients with type 2 diabetes mellitus. *Postgraduate medicine*, *121*(5), 94-107.

Pop-Busui, R., Boulton, A. J., Feldman, E. L., Bril, V., Freeman, R., Malik, R. A., ... & Ziegler, D. (2017). Diabetic neuropathy: a position statement by the American Diabetes Association. *Diabetes Care*, *40*(1), 136-154.

Post, R. E., Mainous, A. G., King, D. E., & Simpson, K. N. (2012). Dietary fiber for the treatment of type 2 diabetes mellitus: a meta-analysis. *The Journal of the American Board of Family Medicine*, *25*(1), 16-23.

Raj, S., & Rajan, G. V. (2017). Correlation between elevated serum ferritin and HbA1c in type 2 diabetes mellitus. *International Journal of Research in Medical Sciences*, *1*(1), 12-15.

Rosso, L. G., Lhomme, M., Meroño, T., Dellepiane, A., Sorroche, P., Hedjazi, L., ... & Chapman, M. J. (2017). Poor glycemic control in type 2 diabetes enhances functional and compositional alterations of small, dense HDL3c. *Biochimica et Biophysica Acta (BBA)-Molecular and Cell Biology of Lipids*, *1862*(2), 188-195.

Rui, L. (2014). Energy metabolism in the liver. *Comprehensive physiology. 4(1): 177–197.*

Sacks, D. B., Arnold, M., Bakris, G. L., Bruns, D. E., Horvath, A. R., Kirkman, M. S., ... & Nathan, D. M. (2011). Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Clinical chemistry*, *57*(6), e1-e47.

Samreen, R., (2009). Diabetes mellitus. Scientific Research and Essays 4(5): 367-373.

Samsom, M., Trivedi, T., Orekoya, O., & Vyas, S. (2016). Understanding the importance of gene and environment in the etiology and prevention of Type 2 diabetes mellitus in high-risk populations. *Oral health case reports*, *2*(1).

Satriano, J., & Vallon, V. (2006). Primary kidney growth and its consequences at the onset of diabetes mellitus. *Amino acids*, *31*(1), 1-9.

Savoldelli, R. D., Farhat, S. C., & Manna, T. D. (2010). Alternative management of diabetic ketoacidosis in a Brazilian pediatric emergency department. *Diabetology & metabolic syndrome*, *2*(1), 41.

Saxena, S., Ruia, S., Prasad, S., Jain, A., Mishra, N., Natu, S. M., ... & Akduman, L. (2017). Increased serum levels of urea and creatinine are surrogate markers for disruption of retinal photoreceptor external limiting membrane and inner segment ellipsoid zone in type 2 diabetes mellitus. *Retina*, *37*(2), 344-349.

Schramm, T. K., Gislason, G. H., Vaag, A., Rasmussen, J. N., Folke, F., Hansen, M. L., ... & Hansen, P. R. (2011). Mortality and cardiovascular risk associated with different insulin secretagogues compared with metformin in type 2 diabetes, with or without a previous myocardial infarction: a nationwide study. *European heart journal*, *32*(15), 1900-1908.

Schwab, U., Lauritzen, L., Tholstrup, T., Haldorsson, T. I., Riserus, U., Uusitupa, M., & Becker, W. (2014). Effect of the amount and type of dietary fat on cardiometabolic risk factors and risk of developing type 2 diabetes, cardiovascular diseases, and cancer: a systematic review. *Food & nutrition research*, *58*(1), 25145.

Seino, Y., Nanjo, K., Tajima, N., Kadowaki, T., Kashiwagi, A., Araki, E., ... & Hanafusa, T. (2010). Report of the committee on the classification and diagnostic criteria of diabetes mellitus. *Journal of diabetes investigation*, *1*(5), 212-228.

Shah, B. R., & Hux, J. E. (2003). Quantifying the risk of infectious diseases for people with diabetes. *Diabetes care*, *26*(2), 510-513.

Sharabi, K., Tavares, C. D., Rines, A. K., & Puigserver, P. (2015). Molecular pathophysiology of hepatic glucose production. *Molecular aspects of medicine*, *46*, 21-33.

Shaw, J. E., Sicree, R. A., & Zimmet, P. Z. (2010). Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes research and clinical practice*, *87*(1), 4-14.

Sollu, M., Banji, D., Otilia, J. F., Vijayalaxmi, C., Srilat, S., & Kumbala, K. (2010). Appraisal on causes and treatment of diabetes mellitus. *Arch App Sci Res*, *2*, 239-260.

Steptoe, A., Hackett, R. A., Lazzarino, A. I., Bostock, S., La Marca, R., Carvalho, L. A., & Hamer, M. (2014). Disruption of multisystem responses to stress in type 2 diabetes: investigating the dynamics of allostatic load. *Proceedings of the National Academy of Sciences*, *111*(44), 15693-15698.

Stevens, J. W., Khunti, K., Harvey, R., Johnson, M., Preston, L., Woods, H. B., ... & Goyder, E. (2015). Preventing the progression to type 2 diabetes mellitus in adults at high risk: a systematic review and network meta-analysis of lifestyle, pharmacological and surgical interventions. *Diabetes research and clinical practice*, *107*(3), 320-331.

Takahashi, K., Kamada, C., Yoshimura, H., Okumura, R., Iimuro, S., Ohashi, Y., ... & Ito, H. (2012). Effects of total and green vegetable intakes on glycated hemoglobin A1c and triglycerides in elderly patients with type 2 diabetes mellitus: the Japanese Elderly Intervention Trial. *Geriatrics & gerontology international*, *12*(s1), 50-58.

Takashi, Y., Koga, M., Matsuzawa, Y., Saito, J., Omura, M., & Nishikawa, T. (2017). Undercarboxylated osteocalcin can predict insulin secretion ability in type 2 diabetes. *Journal of diabetes investigation*.

Tangvarasittichai, S. (2015). Oxidative stress, insulin resistance, dyslipidemia and type 2 diabetes mellitus. *World journal of diabetes*, *6*(3), 456.

Tarr, J. M., Kaul, K., Wolanska, K., Kohner, E. M., & Chibber, R. (2013). Retinopathy in diabetes. In *Diabetes* (pp. 88-106). Springer New York.

Terzin, V., Várkonyi, T., Szabolcs, A., Lengyel, C., Takács, T., Zsóri, G., ... & Czakó, L. (2014). Prevalence of exocrine pancreatic insufficiency in type 2 diabetes mellitus with poor glycemic control. *Pancreatology*, *14*(5), 356-360.

Thompson, C.S. (2013): Diabetic nephropathy: Treatment with phosphodiesterase type 5 inhibitors. *World journal of diabetes 4*(4): 124.

Trinder, P. (1969). Determination of blood glucose using an oxidase-peroxidase system with a non-carcinogenic chromogen. *Journal of clinical pathology*, *22*(2), 158-161.

Trivelli, L. A., Ranney, H. M., & Lai, H. T. (1971). Hemoglobin components in patients with diabetes mellitus. *New England Journal of Medicine*, *284*(7), 353-357.

Tsapogas, P. (2004). Poverty, stress and unmet needs: life with diabetes in the Gaza Governorate. *diabetes voice.*, *49*(2), 12-15.

Tsirona, S., Pappas, C., Kandaraki, E., Kassi, G., Chronopoulou, G., & Diamanti-Kandarakis, E. (2016). Detection of hypoglycemia in type 2 diabetic patients.

Tuligenga, R. H., Dugravot, A., Tabák, A. G., Elbaz, A., Brunner, E. J., Kivimäki, M., & Singh-Manoux, A. (2014). Midlife type 2 diabetes and poor glycaemic control as risk factors for cognitive decline in early old age: a post-hoc analysis of the Whitehall II cohort study. *The lancet Diabetes & endocrinology*, *2*(3), 228-235.

Unger, J. (2012). Uncovering undetected hypoglycemic events. *Diabetes, metabolic syndrome and obesity: targets and therapy*, *5*, 57.

Van Bommel, E. J., Muskiet, M. H., Tonneijck, L., Kramer, M. H., Nieuwdorp, M., & van Raalte, D. H. (2017). SGLT2 Inhibition in the Diabetic Kidney—From Mechanisms to Clinical Outcome. *Clinical Journal of the American Society of Nephrology*, CJN-06080616.

Van Zon, S. K., Snieder, H., Bültmann, U., & Reijneveld, S. A. (2017). The interaction of socioeconomic position and type 2 diabetes mellitus family history: a cross-sectional analysis of the Lifelines Cohort and Biobank Study. *BMJ open*, *7*(4), e015275.

Velázquez-López, L., Muñoz-Torres, A. V., García-Peña, C., López-Alarcón, M., Islas-Andrade, S., & Escobedo-de la Peña, J. (2016). Fiber in diet is associated with improvement of glycated hemoglobin and lipid profile in Mexican patients with type 2 diabetes. *Journal of diabetes research*, *2016*.

Vidal, J., Ibarzabal, A., Romero, F., Delgado, S., Momblán, D., Flores, L., & Lacy, A. (2008). Type 2 diabetes mellitus and the metabolic syndrome following sleeve gastrectomy in severely obese subjects. *Obesity surgery*, *18*(9), 1077.

Vidanelage, M., & Jayasinghe, T. N. (2013). *Effect of Krüppel-like factor 3 on glucose metabolism* (Master's thesis, University of Sydney).

Vitale, M., Masulli, M., Rivellese, A. A., Babini, A. C., Boemi, M., Bonora, E., ... & Clemente, G. (2016). Influence of dietary fat and carbohydrates proportions on plasma lipids, glucose control and low-grade inflammation in patients with type 2 diabetes—The TOSCA. IT Study. *European journal of nutrition*, *55*(4), 1645-1651.

Wanders, A. J., Alssema, M., de Koning, E. J. P., Le Cessie, S., de Vries, J. H., Zock, P. L., ... & de Mutsert, R. (2017). Fatty acid intake and its dietary sources in relation with markers of type 2 diabetes risk. *European journal of clinical nutrition*, *71*(2), 245-251.

Wanner, C., Inzucchi, S. E., Lachin, J. M., Fitchett, D., von Eynatten, M., Mattheus, M., ... & Zinman, B. (2016). Empagliflozin and progression of kidney disease in type 2 diabetes. *New England Journal of Medicine*, *375*(4), 323-334.

Wedick, Nicole M., An Pan, Aedín Cassidy, Eric B. Rimm, Laura Sampson, Bernard Rosner, Walter Willett, Frank B. Hu, Qi Sun, and Rob M. van Dam. "Dietary flavonoid intakes and risk of type 2 diabetes in US men and women." *The American journal of clinical nutrition* (2012): ajcn-028894.

Wewer Albrechtsen, N. J., Kuhre, R. E., Pedersen, J., Knop, F. K., & Holst, J. J. (2016). The biology of glucagon and the consequences of hyperglucagonemia. *Biomarkers in medicine*, *10*(11), 1141-1151.

Wilcox, G. (2005). Insulin and insulin resistance. *Clinical biochemist reviews*, *26*(2), 19.

Wolever, T. M., Gibbs, A. L., Mehling, C., Chiasson, J. L., Connelly, P. W., Josse, R. G., ... & Ryan, E. A. (2008). The Canadian Trial of Carbohydrates in Diabetes (CCD), a 1-y controlled trial of low-glycemic-index dietary carbohydrate in type 2 diabetes: no effect on glycated hemoglobin but reduction in C-reactive protein. *The American journal of clinical nutrition*, *87*(1), 114-125.

World Health Organization (2015): Diabetes Fact Sheet, No. 312. aug 2017; available at: http://www.who.int/mediacentre/factsheets/fs312/en/.

World Health Organization. (2000): Technical report series 894: Obesity: Preventing and managing the global epidemic. Geneva: *World Health Organization*. ISBN 92-4 120894-5.

World Health Organization. (2006). *Prevention of blindness from diabetes mellitus: report of a WHO consultation in Geneva, Switzerland, 9-11 November 2005*. World Health Organization.

Wu, J. H., Micha, R., Imamura, F., Pan, A., Biggs, M. L., Ajaz, O., ... & Mozaffarian, D. (2012). Omega-3 fatty acids and incident type 2 diabetes: a systematic review and meta-analysis. *British journal of nutrition*, *107*(S2), S214-S227.

Xu, F., Zhao, L. H., Su, J. B., Chen, T., Wang, X. Q., Chen, J. F., ... & Wang, X. H. (2014). The relationship between glycemic variability and diabetic peripheral neuropathy in type 2 diabetes with well-controlled HbA1c. *Diabetology & metabolic syndrome*, *6*(1), 139.

Xu, L., Cheema, A., Zarini, G. G., Li, T., & Huffman, F. G. (2017). Interaction Between the Ratio of Polyunsaturated Fat and Saturated Fat Intake and Peroxisome Proliferator-Activated Receptor-γ Coactivator 1-α (PPARGC1A) rs4235308 Polymorphism in Relation to the Risk of Type 2 Diabetes in Cuban American Population. *The FASEB Journal*, *31*(1 Supplement), 644-16.

Yamagishi, S., Fukami K., Ueda S., Okuda, S. (2007): Molecular mechanisms of diabetic nephropathy and its therapeutic intervention. Curr Drug Targets. 8(8): 952-959.

Yassin, M. M., Altibi, H. I., & El Shanti, A. E. (2011). Clinical and biochemical features of type 2 diabetic patients in Gaza Governorate, Gaza Governorate. *West African journal of medicine*, *30*(1), 51-56.

Yau, J. W., Rogers, S. L., Kawasaki, R., Lamoureux, E. L., Kowalski, J. W., Bek, T., ... & Haffner, S. (2012). Global prevalence and major risk factors of diabetic retinopathy. *Diabetes care*, *35*(3), 556-564.

Ye, E. Q., Chacko, S. A., Chou, E. L., Kugizaki, M., & Liu, S. (2012). Greater whole-grain intake is associated with lower risk of type 2 diabetes, cardiovascular disease, and weight gain. *The Journal of nutrition*, *142*(7), 1304-1313.

Yin, J., Yeung, R., Luk, A., Tutino, G., Zhang, Y., Kong, A., ... & Tsang, C. C. (2016). Gender, diabetes education, and psychosocial factors are associated with persistent poor glycemic control in patients with type 2 diabetes in the Joint Asia Diabetes Evaluation (JADE) program. *Journal of diabetes*, *8*(1), 109-119.

Yoneyama, Y., Matsuo, M., Take, K., Kabuta, T., Chida, K., Hakuno, F., & Takahashi, S. I. (2013). The AP-1 complex regulates intracellular localization of insulin receptor substrate 1, which is required for insulin-like growth factor I-dependent cell proliferation. *Molecular and cellular biology*, *33*(10), 1991-2003.

Yuan, H. J., Yang, X. G., Shi, X. Y., Tian, R., & Zhao, Z. G. (2011). Association of serum uric acid with different levels of glucose and related factors. *Chinese medical journal*, *124*(10), 1443-1448.

Zakout A.A. (2006): Non-compliance in type 2 diabetes patients:prevalence and associated factors in Gaza Governorate. Master of Public Health Thesis, Al Quds University, Gaza Governorate, Palestine

Ziaee, A., Afaghi, A., & Sarreshtehdari, M. (2012). Effect of low glycemic load diet on glycated hemoglobin (HbA1c) in poorly-controlled diabetes patients. *Global journal of health science*, *4*(1), 211.

Annexes

Annex 1: Patient questionnaire

Cross sectional study, questionnaire for Clinical and dietary assessment of chronic type-II diabetic patients in Gaza Governorate

أخي المواطن الكريم/ أرجو مساعدتنا في إتمام هذه الدراسة (بحث ماجستير تحاليل طبية / الجامعة الإسلامية) والتي تختص بمرضى النوع الثاني من السكر, حيث أن هدفنا الوقوف على مسبباته، و خاصة علاقته بالغذاء وذلك للحد من مضاعفاته.

Patients and controls Questionnaire

1. Personal profile of the study population:

Name:_____ Serial No:_____

Age:_____ Tel. No : _____

Gender:_____-

_____

Education □University or diploma □Secondary school
□Preparatory school □Primary school
□Illiterate

2. Anthropometric measurement:

Height (cm) : _____ Weight (kg):_____
Body Mass Index: _

3. Socioeconomic data of the study population:

- Employment: □Yes □No
- Family income: <1000 Shekels …….1000-2000 Shekels ……
  >2000 Shekels …….
- Family history for Type 2 diabetes □Yes □No
- Smoking: □Yes □No
- Physical activity: □Yes □No
- Compliance of medication **(only for patients)**: □Yes □No
- Duration of Type2 Diabetes mellitus/years:**.(only for patients)** _____ year
- Regular blood glucose monitoring □ Yes □ No
  - If yes □daily □weekly □monthly

4. Self-reported complications:

Cardiovascular diseases □Yes □No
Retinopathy □Yes □No
Neuropathy □Yes □No

5.Type of treatment .

MetFormin □Yes □No

Glibenclamidine □Yes □No

data

نوع الطعام	مرة اسبوعيا	مرتين	اكثر من مرتين
لحوم			
أسماك			
فواكه			
خضروات			
ألبان و مشتقاتها			
بقول			
مقالي			
حلويات			
زيت زيتون			

Agreement:

I agree to complete this questionnaire concerning my health statement.

أنا موافق/ ة على تعبئة هذا الاستبيان الذي يتعلق بصحتي.

التوقيع: .....
التاريخ: .....

شكرا لكم على حسن تعاونكم

الباحثة/ ميساء رضوان ابو الخير

Annex 2: Ministry of health permission letter

State of Palestine
Ministry of health

دولة فلسطين
وزارة الصحة

السيد : ناصرالدين رافت مصطفى ابوشعبان المحترم التاريخ:05/12/2016

مدير عام بالوزارة/الإدارة العامة لتنمية القوى البشرية - /وزارة الصحة

السلام عليكم ,,,

الموضوع/ تسهيل مهمة باحثة/ ميساء ابوالخير

التفاصيل //
بخصوص الموضوع أعلاه، يرجى تسهيل مهمة الباحثة/ **ميساء رضوان أبو الخير**
الملتحقة ببرنامج ماجستير الأحياء الدقيقة- كلية العلوم – الجامعة الإسلامية بغزة في إجراء بحث بعنوان - :
"Clinical and dietary Assessment of Chronic type 2 diabetic patients in Gaza Governorate"
حيث الباحثة بحاجة لتعبئة استبانة وأخذ قياسات الطول والوزن وجزء من عينة دم سحبت لأغراض تشخيصية من عدد من مرضى السكر النوع الثاني المراجعين لمراكز الرعاية الاولية في مدينة غزة.
نأمل توجيهاتكم لذوي الاختصاص بضرورة الحصول على الموافقة المستنيرة من المرضى اللذين هم على استعداد للمشاركة في البحث من ثم تمكين الباحثة من التواصل معهم، ووفق الضوابط الخاصة المعمول بها في الوزارة فيما يتعلق بعينات الدم وعلى مسولية الباحثة،، بما لا يتعارض مع مصلحة العمل وضمن أخلاقيات البحث العلمي، و دون تحمل الوزارة أي أعباء أو مسئولية .وتفضلوا بقبول التحية والتقدير،،،

محمد ابراهيم محمد السرساوي
/الإدارة العامة لتنمية القوى البشرية -

التحويلات

■ محمد ابراهيم محمد السرساوي(مدير دائرة)	← ناصرالدين رافت مصطفى ابوشعبان(مدير عام بالوزارة)	إجراءاتكم بالخصوص( )
■ ناصرالدين رافت مصطفى ابوشعبان(مدير عام بالوزارة)	← فؤاد عبد الحليم توفيق العيسوي(وكيل وزارة مساعد)	إجراءاتكم بالخصوص( )
■ فؤاد عبد الحليم توفيق العيسوي(وكيل وزارة مساعد)	← حسناء احمد محمد الشريف(مدير دائرة)	لعمل اللازم( )

Gaza Tel. (+970) 8-2846949 Fax. (+970) 8-2826295
غزة تلفون (+970) 8-2846949 فاكس (+970) 8-2826295

Annex 3: Helsinki committee letter

المجلس الفلسطيني للبحث الصحي

Palestinian Health Research Council

تعزيز النظام الصحي الفلسطيني من خلال مأسسة استخدام المعلومات البحثية في صنع القرار

Developing the Palestinian health system through institutionalizing the use of information in decision making

Helsinki Committee

For Ethical Approval

Date: 2017/08/27 **Number:** PHRC/HC/251/17

Name: MAYSA R. ABUELKHAIR الاسم:

We would like to inform you that the committee had discussed the proposal of your study about:

نفيدكم علماً بأن اللجنة قد ناقشت مقترح دراستكم حول:

Clinical and dietary assessment of chronic type-II diabetic patients in Gaza Governorate.

The committee has decided to approve the above mentioned research. Approval number PHRC/HC/251/17 in its meeting on 2017/08/27

و قد قررت الموافقة على البحث المذكور عاليه بالرقم والتاريخ المذكوران عاليه

Signature

Member **Member**

Chairman

Genral Conditions:-

1. Valid for 2 years from the date of approval.
2. It is necessary to notify the committee of any change in the approved study protocol.
3. The committee appreciates receiving a copy of your final research when completed.

Specific Conditions:-

E-Mail:pal.phrc@gmail.com

Gaza - Palestine غزة - فلسطين

شارع النصر - مفترق العيون