An-Najah National University

Faculty of Graduate Studies

Prevalence and Associated Factors of Diabetic Retinopathy among Diabetic Patients in the West Bank: A Cross Sectional Study

By

Ibrahim Abdullah Taha

Supervisor

Dr. Hamzeh Al Zabadi

This Thesis is Submitted in Partial Fulfillment of the Requirements for The Degree of Master in Public Health, Faculty of Graduate Studies, An-Najah National University, Nablus-Palestine.

2018

Prevalence and Associated Factors of Diabetic Retinopathy among Diabetic Patients in the West Bank: A Cross Sectional Study

By

Ibrahim Abdullah Taha

This Thesis was Defended Successfully on 23/ 5/ 2018 and approved by:

Defense Committee Members	Signature
1. Dr. Hamzeh Al-Zabadi / Supervisor	.....
2. Dr. Nuha El-Sharif / External Examiner	.....
3. Dr. Liana Al-Labadi / Internal Examiner	.....

Dedication

All praises to **Allah**, Today I fold a days of tiredness days were very beautiful despite the difficult circumstances. To utmost knowledge lighthouse to our greatest and honored **prophet Mohammed**- Peace be upon him.

To my other soul, who spent the nights in order to be what I am today to my beloved **Mother**.

To whom he strives to bless comfort and welfare, to my first inspiration, who supported me and stood beside me always, to my beloved **Father**.

To those who were very proud of me, to the blood that is in my veins, to my **brothers** and the flower of our house my **sister**.

To those who taught me letters of gold, and words of gems, to those who gave me so much, to my **teachers**.

To the comrades of the path, to those who always supported me, to the shining candles in my life to my **friends** and my **colleagues**.

To my country **Palestine**, To my beloved **university**, to the spirit of martyrs and prisoners.

Acknowledgments

Firstly, I must thank God (Allah) for his graces and blessing on me to complete this thesis.

I would like to express my thanks and gratitude to my supervisor Dr. Hamzeh.

Al Zabadi for his encouragement and great guidance throughout this study.

I would also like to thank Dr. Yousef Al-Shanti for everything he has provided to us in this research.

Thanks also to both of Dr. Adnan Bustami, Dr. Reham Shehadeh, Mr. Rami Othman, Dr. Liana Al Labadi, Dr. Seif Malhas.

Thanks also to An-Najah National University, the Palestinian Ministry of Health and Nablus city Charitable Medical Complex.

الإقرار

أنا الموقعة ادناه، مقدمة الرسالة التي تحمل العنوان:

Prevalence and Associated Factors of Diabetic Retinopathy among Diabetic Patients in the West Bank: A Cross Sectional Study

أقر بأن ما اشتملت علية هذه الرسالة انما هو نتاج جهدي الخاص، باستثناء ما تمت الإشارة اليه حيثما ورد، وأن هذه الرسالة كاملة، أو أي جزء منها لم يقدم من قبل لنيل أي درجة أو لقب علمي أو بحثي لدى أي مؤسسة أو بحثية أخرى.

Declaration

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

Student's Name: إسم الطالب: ابراهيم عبد الله ابراهيم لحه

Signature: التوقيع

Date: التاريخ: 23/5/2018

Table of Contents

List of Tables

List of appendices

List of Abbreviations

AGEs	Advanced glycation end products
BCVA	Best corrected visual acuity
BM	Basement Membrane
BMI	Body mass index
BRB	Blood Retinal barrier
CSME	Clinically significant macular edema
CWS	Cotton wall spots
DM	Diabetes mellitus
DR	Diabetic retinopathy
ETDRS	Early treatment diabetic retinopathy study
FFA	Fundus fluorescein angiography
ICO	International council of ophthalmology
IOP	Intraocular pressure
NPDR	Non proliferative Diabetic Retinopathy
OCT	Optical coherence tomography
PDR	Proliferative Diabetic Retinopathy
RAS	Retina-angiotensin system
ROS	Reactive oxygen species
RPE	Retinal pigment epithelium
SPSS	Statistical pack-age for social sciences
UAE	United Arab Emirates
UKPDS	UK prospective diabetes study
VTDR	Vision-threatening diabetic retinopathy
WESDR	Wisconsin Epidemiologic Study of Diabetic Retinopathy
WHO	World health organization
HbA1c	Glycated Hemoglobin
TG	Triglycerides
CHOL	Cholesterol
HDL	High density lipoprotein
LDL	Low density lipoprotein
ALK PHOS	Alkaline phosphatase

GOT	Glutamic-Oxaloacetic Transaminase
GPT	Glutamic-Pyruvic Transaminase
CREAT	Creatinine
BU	Blood Urea
VEGF	Vascular Endothelial Growth Factor
MoH	Ministry of Health
PHC	Primary Health Centers

Prevalence and Associated Factors of Diabetic Retinopathy among Diabetic Patients in the West Bank: A Cross Sectional Study

By

Ibrahim Abdullah Taha

Supervisor

Dr. Hamzeh Al Zabadi

Abstract

Introduction: Diabetic retinopathy (DR) is one of the complications associated with uncontrolled DM. DR is a leading preventable cause of visual impairment in the world and is also the leading cause of blindness in adults under 75 years of age in developing countries. We aimed to explore the prevalence and associated risk factors of DR among diabetic patients in the West Bank.

Materials and Methods: A quantitative cross-sectional study was conducted in all West Bank cities. All patients underwent a comprehensive eye exam in addition to blood and urine tests. Early treatment of diabetic retinopathy study (ETDRS) questionnaire was used for data collection from all patients.

Results: Prevalence of all DR in West Bank was 41.8%, While the prevalence of NPDR was 50.3% (Mild NPDR 38.5%, 10.6% for moderate NPDR and 1.2% for severe NPDR), PDR was 9.9% and 39.7% for DME (mild DME was 17.4%, moderate DME 15.5% and severe DME was 6.8%). Prevalence of vision threatening (PDR, DME) was 49.7%.

univariate analysis had shown that DR were significantly associated with BMI (P = .035), DM duration (P = .002), LDL (P = .034), GOT level (P = .016) and BU (P = .044). Multivariate analysis have shown a strong significant association between diabetic retinopathy with DM duration ($P < 0.05$), abnormal levels of LDL (P = 0.008), abnormal levels of GOT ($P < 0.05$), and Overweight ($P < 0.05$).

Conclusion: Earlier diagnosis of diabetes and DR can help to control some of DR factors and prevent further complications and vision loss. Population-based educational programs on diabetes and diabetic retinopathy and continuous medical education on diabetes management can improve diabetes care and self-management and prevent eye complications.

Chapter One
Introduction

1.1 Background

Diabetes mellitus is a chronic disease that through its complications can seriously impact the quality of life of individuals. There are warnings from the World Health Organization (WHO) that the number of people with diabetes is rapidly increasing. The recent studies showed that prevalence of diabetes mellitus worldwide was 6.4% (285 million) in 2014, and will increase to 7.7% (439 million) by 2030 (Mihardja et al., 2014). Diabetes is an important health problem because of its high morbidity and mortality. There are many complications associated with diabetes including macrovascular disease that involves, cardiovascular and peripheral vascular disease and/or microvascular complications including neuropathy, nephropathy, and retinopathy (Jenkins et al., 2010).

Diabetic retinopathy (DR) is one of the leading preventable causes of visual impairment in the world, and one of the complications associated with uncontrolled DM. Treatment and early detection can help to prevent any additional consequent ocular complications (Katibeh et al., 2015).

The worldwide prevalence of DR is 34.6%. In developed countries, DR is the leading cause of blindness in adults under 75 years of age (Joanne et al, 2013).

It is a progressive disease affecting mainly the integrity of microscopic vessels found in the retina. At first, DR may cause no symptoms or only

mild vision problems. Eventually, it can lead to visual impairment and blindness (Schmidt et al., 2010).

1.2 Significance of the study

Diabetic retinopathy (DR) is one of the leading preventable causes of visual impairment in the world. Therefore, treatment and early detection can help preventing any complications that might happen as a result from this disease (Rayn lee et al., 2015).

There is a warning from the World Health Organization that the prevalence of diabetic retinopathy is increasing worldwide, especially in developed countries (WHO, 2016). The WHO stated that there is a need to establish screening and surveillance programs to detect diabetic retinopathy in early stages as the early detection might help to prevent deterioration of this disease (Squirrell et al., 2013).

Diabetic retinopathy, therefore, should be considered as a serious public health issue that is worthy of diagnosis and effective early intervention and treatment. To the best of our knowledge, our present study is the first one conducted in Palestine among general population (WHO, 2016).

1.3 Study Objectives

1.3.1 General objective

To explore to what extent diabetic retinopathy (DR) is prevalent among diabetic patients in the West Bank in 2017, and to address its associated risk factors.

1.3.2 Specific objectives

1. To diagnose DR among diabetic patients in whole West Bank Governorates by an ophthalmologist based on both signs and symptoms.
2. To assess DR severity and stages by an ophthalmologist based on both signs and symptoms
3. To examine how DR is associated with demographical variables such as sex and age.
4. To identify the associated risk factors related to diabetic retinopathy development.
5. To identify any ocular complications associated with diabetic retinopathy such as cataract, glaucoma and robiosisiridies.

Chapter Two
Theoretical framework

2.1 Pathophysiology of diabetic retinopathy

Retina consists of huge number of cells, normal vision depends on the integrity of these cells and intact cell – cell communication. Before any diabetic damage, all retinal cells are activated and produce number of mediators, such as growth factors, coagulation factors, vasoactive agents and adhesion molecules (Juan Wang et al., 2015).

The production of these mediators leads to increase retinal blood flow, increase capillary permeability, altered cell turnover (apoptosis, proliferation and hypertrophy) and tissue remodeling (Pelinikanova et al., 2016). Diabetes mellitus damages all the major cells through the layers of the retina. Neurons (photoreceptors, bipolar, horizontal and ganglions), glia (Muller cells and astrocytes), microglia, pigment epithelial cells and and significantly the vascular cells (Vecino et al., 2016).

Diabetic patients have high systemic levels of glucose, lipids, hormones, amino acids and inflammatory molecules. the increase systemic, vitreal and retinal levels of these factor induced several unrelated and inter-related biochemical pathways implicated in pathophysiology of the disease (Anjana et al., 2014).

Several studies such as UK prospective diabetes study (UKPDS) suggest that hyperglycemia is the initial cause of diabetic retinopathy,

hyperglycemia in retinas activates formation advanced glycation end products (AGEs), polyol formation, increased hexosamine flux, activation of the retina-angiotensin system (RAS) and production of excess reactive oxygen species (ROS) (UKPDS, 2012).

The increase of these factors especially fluxes through these pathways may leads to increase promotion of apoptosis, inflammations and angiogenesis. This may induce damage of the retinal cells and tissues and leads to diabetic retinopathy. In early stages of diabetic retinopathy alteration in retinal blood flow and Blood-Retinal Barrier Dysfunction occur (Semeraro et al.,2014). The progression of the disease goes through the following phases:

Alteration in retinal blood flow

Several studies such Berthold Pemp et al., study suggest that Elevated glucose levels may be the initial factor leading to alterations of vessel architecture in the retina, perfusion abnormalities, and progression of the disease. This study compared blood flow of diabetic patients with other without diabetes. They found that blood flow increase in the case of diabetes, they suggest that increase of glucose in blood leads to increase plasma density, high density of plasma cause high velocity of blood flow, With the passage of time these high blood flow causes alteration of vessel architecture in the retina, perfusion and then new micro blood vessel appear. In general, the majority of recent studies have proven this theory of retinal flow (Berthold P et al.,2016).

Blood-Retinal Barrier Dysfunction occur

The earliest and most significant change in diabetic retinopathy (DR) is blood-retinal barrier (BRB) dysfunction, the blood-retinal barrier is divided into an inter and an outer barrier. The inner part is formed by the tight junctions of retinal capillary endothelial cells covered with glial cells which is muller cells (Cunha Vas et al., 2011). the function of the inner division is to nourish the inner tow- third of human retina and remove toxic molecules and compounds. While the outer division of the BRB consists of the tight junction of the retinal pigment epithelial cells (RPE) (Renee Bozard et al., 2010). The retinal pigment epithelium (RPE) closely interacts with photoreceptors in the maintenance of visual function. The RPE transports ions, water, glucose and metabolic end products (Wen R, Song et al,.2011). RPE can be disrupted by inflammatory and oxidative changes associated with hyperglycemia. The changes in Long term lesions of diabetic retinopathy include Basement membrane thickening, microaneurysms and neurodegeneration and glial dysfunction (Cunha Vas et al., 2011).

Basement membrane thickening

Vascular basement membrane (BM) thickening is a fundamental structural alteration of small blood vessels in the retina. In diabetes, early hyperglycemia is sufficient to increase the synthesis of basement membrane components in the retina. this thickening occurs during collagen and fibronectin synthesis, in the case of hyperglycemia the synthesis of

collagen and fibronectin increase leading to thickening of basement membrane of retinal vessels (Roy Stare et al., 2010). Diabetic basement membrane thickening appears to involve qualitative alterations of specific basement membrane markers at an advanced disease stage. Several studies suggested that basement membrane thickening may contribute to accelerated vascular cell death and vessel instability in the diabetic retina (Hainsworth et al., 2010).

Microaneurysms

Capillary microaneurysms are normally the first clinically recognizable feature of diabetic retinopathy. Microscopically, microaneurysms are present as ‘balloon-like’ outpunching’s of the capillary (Tam J et al., 2012). Microaneurysms occurs result from extensive accumulation of inflammatory cells resulting from diabetes. These inflammatory cells damage the endothelium and it is apparent that later-stage microaneurysms are invariably without an endothelial lining (Peramaiyan et al., 2013).

Neurodegeneration & Glial dysfunction

Changes mentioned before leads to retinal neuronal degeneration as diabetes progresses. Recent research has been conducted indicate a range of neural retina abnormalities ranging from neurotransmitter changes to overt loss of retinal ganglion cells, amacrine cells or even photoreceptors (Helga Kolb et al., 2009). There is also a highly complex interplay between neurons, glia and vascular components of the retina and diabetes is likely to profoundly alter the function of these cell interactions (Xu Heping et al., 2011).

2.2 Stages and classification of Diabetic Retinopathy

DR can be divided into three clinical stages according to early treatment diabetic retinopathy study (ETDRS) classification which is: non-proliferative diabetic retinopathy (NPDR), proliferative retinopathy (PDR) and maculopathy (ETDR, 2016).

Non-proliferative diabetic retinopathy (NPDR)

During nonproliferative (NPDR) the early and mild sign is the formation of microaneurysms i.e. outward ballooning of the capillary walls, at this stage of microaneurysms the area affected is the area located temporal to the vision area which is called (fovea) and they are usually asymptomatic when they first arise, Further signs of non-proliferative diabetic retinopathy of increasing severity from moderate to severe. at moderate stage the vascular changes seen in one or two quadrant of the retina and the vessels that nourish the retina, these may swell and distort, also may lose their ability to transport the blood. the severe stage seen at more than two quadrant of the retina also more vessels are affected and blocked, atthis stage, these areas secrete growth factors that signal the retina to grow new blood vessels this called neovascularization (ETDRS, 2016).

Proliferative retinopathy (PDR)

The second stage which is proliferative diabetic retinopathy (PDR) including more neovascularization along the inside surface of the retina and into the vitreous gel, the fluid that fills the eye. The new blood vessels are

fragile, which makes them more likely to leak and bleed away from a wall. Retinal detachment and scars might cause visual loss and permanent blindness (ETDRS, 2016).

Diabetic Maculopathy (DME)

The third stage is maculopathy which is the last stage of diabetic retinopathy, clinically significant macular edema (CSME) occurs if there is thickening of the retina involving the center of the retina (macula) or the area within 500 μm of it, if there are hard exudates at or within 500 μm of the center of the retina with thickening of the adjacent retina, or if this thickening occurs at the level of optic disk. The International Clinical Diabetic Macular Edema Disease Severity Scale includes two major levels: absent and present. If DME is present, it is divided into mild (some retinal thickening or hard exudates in the posterior pole, but distant from the center of the macula), moderate (retinal thickening or hard exudates approaching the center of the macula but not the center), and severe (involving retinal thickening or hard exudates involving the center) (ETDRS, 2016). Table (1) shows Summary of the stages of diabetic retinopathy according to ETDRS.

Table (1): Summary of the stages of diabetic retinopathy according to ETDRS.

The stage	Retinal change	
NPDR	Mild NPDR	microanurysms at temporal retina
	Moderate NPDR	seen in one or two quadrant of the retina and the vessels
	Severe NPDR	seen at more than two quadrant of the retina , more vessels are affected and blocked , new vessels are appear and Cotton wall spots
PDR	Neovascularization at the retina cause scars and retinal detachment	
Maculophathy	Mild	some retinal thickening or hard exudates in the posterior pole, but distant from the center of the macula
	Moderate	retinal thickening or hard exudates approaching the center of the macula but not the center
	Severe	involving retinal thickening or hard exudates involving the center

2.3 Examination and diagnosis of diabetic retinopathy (DR)

According to International Council of Ophthalmology (ICO), the diagnosis of diabetic retinopathy should Passes through these procedures:

-Patients history

A proper diabetic eye exam should always begin by gathering a thorough history from the patient we should ask about diabetic duration, past glycemic control (HbA1c), medication especially insulin oral hypoglycemic, antihypertensive, and lipid-lowering, blood pressure, cholesterol level and renal status (ICO, 2016).

- Initial Physical Exam

Examination should begin with visual acuity VA, intraocular pressure IOP and slit-lamp exam, including careful inspection of iris neovasultization, if iris neovasultization present gonioscopy should be performed to assess the iridocorneal angle (ICO, 2016).

- Fundus Examination Assessment Methods

Currently, the two most sensitive methods for detecting DR are retinal photography and slit-lamp bio microscopy through dilated pupils. Both depend on interpretation by trained eye health professionals. Fundus photography has the advantage of creating a permanent record, and for that reason, it is the preferred method for retinopathy assessment. However, well- trained observers can identify DR without photography and there are many situations in which that would be the examination of choice.

The use of all instruments requires training and competence but more skill is needed for indirect ophthalmoscopy and slit-lamp biomicroscopy than for fundus photography. Newer, semi-automatic non-mydriatic fundus cameras can be very easy to use. Media opacities will lead to image/view degradation and all photographs/images must be reviewed by trained personnel. However during these tests, We should exclude any retinal or virtuous abnormalities such as blots or spots, cotton wall spots (CWS), neovasultization, abnormalities in optic disk and macular edema (ICO, 2016).

- Fundus fluorescein angiography (FFA)

Other tests may be conducted for most accurate results such as Fundus fluorescein angiography (FFA), in this test special dye will inject into patient arm then pictures will have obtained as the dye circulates through your eyes. At this test doctor can use the images to pinpoint blood vessels that are closed, broken down or leaking fluid(ICO, 2016).

- Optical coherence tomography (OCT)

We can also use optical coherence tomography (OCT) exam which will help to determine whether fluid has leaked into retinal tissue, this imaging test provides cross-sectional images of the retina that show the thickness of the retina. At this test we can make sure if any macular edema presence or not (ICO, 2016).

Chapter Three
Literature review

3.1 Previous Studies

3.1.1 Prevalence of diabetic retinopathy globally

Several studies are conducted to estimate the prevalence and associated risk factors of diabetic retinopathy (DR). One of the main studies was that conducted by Joanne W.Y. et al, to estimate the global prevalence of diabetic retinopathy (DR) among diabetic patients. During this study a pooled analysis using individual participant data from population-based studies around the world was performed, this study collected a total of 35 studies (1980–2008) provided data from 22,896 individuals with diabetes. The overall prevalence was 34.6% for any DR. At this study, they found that the prevalence of DR increased with diabetic duration, hemoglobin A(1c), blood pressure levels and were higher in people with type 1 compared with type 2 diabetes (Joanne et al., 2009).

3.1.2 Prevalence of diabetic retinopathy in USA

One of the most important studies also is a cross-sectional study conducted by Xinzhi Zhang et al., between 2005-2010 to estimate the prevalence of DR in United States. The sample size was 1006 diabetic patients aged between (20-79) years old. The results of this study showed that the prevalence of DR in United States was 28.5%. The prevalence among men was slightly more than women by an odds ratio of 2.7 as well as higher prevalence was found among patients with hemoglobin A1c level more

than 7 by odds ratio of 1.45 compared to those with hemoglobin A1c level of less than7. Odds ratio of hypertension was 1.3 than patients without hypertension(Xinzhi et al., 2012).

In the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), the prevalence was 40%. for patients ages 30 and younger, proliferative diabetic retinopathy (PDR), the most vision-threatening form of the disease, was present in approximately 50% of Type 1 patients who had the disease for 20 years.

3.1.3 Prevalence of diabetic retinopathy in Europe Countries

In UK, the prevalence of DR according to Martin C. Gulliford et.al was 22.5%.This study conducted between (2009- 2012). The sample size in this study was 2762. Risk factors such as Age, HbA1c, hypertension, Body mass index (BMI), low density Lipoprotein (LDL) and high density Lipoprotein (HDL) were studied. Odds ratio was higher in patients who aged more than 60 years by 1.6. The odds were higher also among patients with HbA1c more than 7 by 1.87 (Martin et al., 2014).

In France, according to Massin Peter et al, the prevalence of diabetic retinopathy was 32.2%, and it is close to the results in UK according to study conducted in 2009 (Massin P et al., 2009).

The eye clinic of Linköping University Hospital in Sweden conducted a study to determine the prevalence of diabetic retinopathy in whole country. The prevalence of any DR was 41.8% (95% CI 38.9-44.6) for patients with

type 1 diabetes and 27.9% (27.1-28.7) for patients with type 2 diabetes (Emilie Hentz et al., 2010).

3.1.4 Prevalence of diabetic retinopathy in Africa

A study conducted in Africa collected 62 studies from 21 African countries by Burgess P.I, et al. This study collected many types of study designs which were two cohort studies; five case–control studies, 32 diabetes clinic-based, 9 eye clinic-based and 11 other hospital-based surveys. The reported prevalence range for diabetic retinopathy was 7.0 to 62.4%, proliferative diabetic retinopathy 0 to 6.9%, and non-proliferative diabetic retinopathy ranged from 1.2 to 31.1%. During this study, the focus was on the income level of these countries. No obvious association between prevalence and income level of the country was detected (Burgess et al., 2012).

3.1.5 Prevalence of diabetic retinopathy in Asia

In Asia also, several studies were conducted. Ji-Hyun Kim et al. conducted a cross-sectional study to investigate the prevalence of diabetic retinopathy and its associated factors in rural Korean patients with type 2 diabetes, the study was conducted during (2005-2006) in 687 eligible participants aged over 40 years with type 2 diabetes . The overall prevalence of diabetic retinopathy was 18%, proliferative or severe non-proliferative was found in 5.0% of the study subjects (Ji-Hyun et al., 2008).

Another cross-sectional study consisting of 217 diabetic patients conducted by Tajunisah I et al. to estimate the prevalence of DR in Malaysia, the results showed that the prevalence of DR in Malaysia was 51.6% (Tajunisah et al., 2015).

3.1.6 Prevalence of diabetic retinopathy in Middle East

In the Middle East, however, the prevalence of DR in Saudi Arabia was 31.5% according to Ataur Rahman Khan et al. At this study the odd ratios of DR among diabetic residing in an urban area was significantly higher than diabetics residing in rural areas OR = 1.94, DR was associated to the duration of diabetes OR = 1.70, uncontrolled blood sugar level OR = 1.96 (Ataur et al., 2011).

In the United Arab Emirates (UAE), the prevalence was 19%, most of patients were males by 74%. Type I DM was a highly significant contributing risk factor (82.6%) for type 1 (16.4%) vs for type 2 (Fatma et al., 2011).

A study in Iran found that the prevalence of DR was 23.6% according to cross-sectional study performed on 1022 diabetic participant (Heydari et al., 2012).

The prevalence of DR In Oman was the highest on of the Arabic countries and found to be 66.4 %, this results according to cross-sectional study conducted by el Haddad OA et al., mild prevalence was 25.6%, moderate-severe NPR (Non Proliferative retinopathy) was 4%, and proliferative

diabetic retinopathy prevalence was 12.8% (El Haddad et al., 2012) .

In Jordan, a study conducted by Maha Titi et al. found that the prevalence of DR among diabetic patients attended to Jordan university hospital in the period between (Jan 2014 to Dec 2014) was 64.1%. They used a cross-sectional study design on 1961 diabetic patients and had shown that old age group, long duration of diabetes, poor glycemic control, uncontrolled blood pressure and the presence of nephropathy were significantly associated with diabetic retinopathy (Maha titi et al., 2013). The prevalence of diabetic retinopathy in Middle East countries are summarized below in the table (2).

Table (2): Prevalence of diabetic retinopathy in Middle East countries.

Country	Prevalence	Reference (author's)	Year of publication
Saudi Arabia	31.5 %	Ataur Rahman Khanet al.,	2010
UEA	19%	Fatma Al-Maskariet al.,	2011
Yemen	55%	Mahfouth A Bamashmuset al.,	2009
Kuwait	Up to 40%	Al-Adsani AM.	2010
Jordan	up to 64%	Mahatitiet al.,	2013
Iraq	37%	Amani na'maet al.,	2000
Iran	23%	Heydari Bet al.,	2015
Bahrain	Up to 25 %	Jameel Nasser et al.,	2010
Egypt	20%	Macky TAet al.,	2007
Oman	66.4%	el Haddad OAet al.,	2012

One of the most important limitations in these studies is that they do not conduct laboratory tests by themselves but they took the data from medical records. Some of them also used different lab tests devices through the same research. The prevalence of DR ranged from 7% in Norway to 66.4% in Oman (Klistad et al., 2012: El-hadad et al., 2012).

Chapter Four
Materials and Methods

4.1 Study design, population and settings

A quantitative cross–sectional study was conducted. The study population of DM patients in West Bank in 2016 was estimated to be around 278,302 patients according to the Palestinian Ministry of Education (PMoH)(MOH, 2016). Subjects were selected from the DM patients who were above 18 years of age and were followed up in Palestinian ministry of health (MoH) centers. Subjects were recruited in the primary health care centers (PHC) of the MoH in all West Bank directorates (Jenin, Tulkarm, Qalqelia, Nablus, Salfit, Tubas, Ramallah, Bethlehem, Jericho, and Hebron). PHC centers of MoH were chosen due to their accessibility and representativeness to the majority of DM patients in the West Bank. In addition, 422 of 608 PHC centers are provided by MoH so it is considered as the major healthcare provider for DM patients in the West Bank and the vast majority of DM patients seek healthcare in the governmental sector as those patients are usually insured. It should be noted that 189916 families are having governmental insurance. DM patients with cognitive dysfunction or refused to participate were not included.

4.2 Sample size

Subjects were recruited by random proportional method. The sample size was calculated using the following equation (Charan J et al.,2013):

$$ss = \frac{Z^2 * (p) * (1-p)}{c^2}$$

Z = Standard normal variate (1.96 for 95% confidence level).

p = Expected proportion in population.

c = Absolute error.

We used a standard normal variate of 1.96 and an absolute error of 5%. However, there were no previous researches in Palestine regarding this topic so we assume the expected proportion in population (p) to be 0.5 in order to have the highest sample size. After inserting these figures into the previously mentioned equation, the total sample was 385. Distribution of sample between West Bank directorates depended on proportion of each directorate DM patients from the total West Bank DM patients excluding those under 18 years old. Therefore, 83 patients were chosen from Nablus, 77 patients from Hebron, 58 patients from Jenin, 48 patients from Tulkarm, 39 patients from Ramallah, 24 patients from Bethlehem, 17 patients from Qalqelia, 16 patients from Jerusalem, 9 patients from Salfit, 9 patients from Tubas, 5 patients from Jericho.

4.3 Variables operational definitions

Education level: Those who cannot read or write considered as not educated, who completed elementary education considered as primary education, who completed secondary education considered secondary education, who continued beyond secondary considered as high education.

BMI group*:* Underweight: in case of BMI < 18.5, normal weight: in case of 18.5 ≤ BMI < 25, overweight in case of 25 ≤ BMI < 30, and obesity if BMI ≥ 30.

Directorate category*:* North West Bank includes Nablus, Jenin, Tulkarm, Qalqelia, and Tubas, Middle West Bank includes Salfit, Ramallah and Al Berih, Jerusalem, and Jericho, South West Bank includes Hebron and Bethlehem.

DM type: Type 1 DM or Type 2 DM.

DM treatment: No treatment, diet only, oral hypoglycemic agents only, insulin only, combination of diet and oral hypoglycemic agents, combination of diet and insulin, combination of oral hypoglycemic agents and insulin, combination of diet and oral hypoglycemic agents and insulin.

Hypertension: Systolic BP ≥140 mm Hg or a diastolic BP ≥ 90 mm Hg or undergoing antihypertensive therapy.

Current smoking: Smoking more than one cigarette per day or one shisha per week for at least one year.

Systemic steroid therapy: Using systemic steroid for at least one year.

Ocular trauma*:* Any history of physical or chemical or radiation trauma in either eye or both eyes.

Topical steroid therapy*:* Using ocular topical steroid for at least one month in either eye or both eyes.

Retinopathy treatment*:* No history of treatment, history of injection only, history of LASER only, history of surgery, history of injection and LASER, history of injection and surgery, history of LASER and surgery, history of injection and LASER and surgery in either or both eyes.

4.4 Data collection procedure

Subjects were first recruited. The procedure of recruitment was as following: a list of diabetic patients in each directorate was obtained from MoH, subjects were randomly selected from each directorate by using random sampling technique. After that, subjects were called by phone to tell them about participation in this research, subjects were motivated to participate by telling them that their participation will be free screening for cataract and lab tests will be done by qualified team. Subjects in each directorate were told about the time and PHC center which is the main center for directorate.

The selected subjects were interviewed face to face for an average of ten minutes to fill the study's previously modified validated Early Treatment Diabetic Retinopathy Study (ETDRS) questionnaire (ETDRS, 2016). Then, blood and urine sample were obtained and then after, subjects underwent pupil dilation by using a mydriatic agent (Mydramide is a Tropicamide 5% which produced by (Dr. Fischer company), one drop for each eye. Twenty to thirty minutes after that, dilated eye exam done by the ophthalmologist using Top-Con Slit-Lamp and then the results were documented based on

the ETDRS Classification System of Diabetic retinopathy to Present of NPDR, PDR and Maculopathy (ETDRS, 2016).

The modified questionnaire was composed of 5 sections; (1) socio-demographic data including age, sex and directorate; (2) medical history including weight and height, DM type, DM duration and treatment, history of hypertension, history of systemic steroid therapy; (3) ocular history including ocular trauma or topical steroid therapy or retinopathy treatment; (4) ophthalmic examination results using slit-lamp according to ophthalmologist findings regarding cataract and its types and stages if present; (5) blood, serum and urine laboratory tests performed by the research team in Nablus city Charitable Medical Complex. Laboratory tests included: Glycated Hemoglobin (HbA1c), Triglycerides (TG), Cholesterol (CHOL), High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), Alkaline Phosphatase (ALK PHOS), Glutamic-Oxaloacetic Transaminase (GOT), Glutamic-Pyruvic Transaminase (GPT), Creatinine (CREAT), Blood Urea (BU), and Microalbumuria (MALB).

4.5 Laboratory procedures

Blood and urine samples were obtained from patients according to the recommendations of manufacturer of used kits.

Blood sample was taken at fasting status for 8-10 hours by vacutainer blood tubes (4 ml clot activator tube and 3 ml EDTA tube) for each patient, urine sample was taken as random midstream around 50 ml volume.

All samples were stored by sample transporter box at temperature 2-8 Celsius till reached the lab, where urine and clot activator samples were centrifuged to prepare urine and serum for tests.

EDTA tube whole blood was analyzed by HumaMeter A1c system which is a product of Human Germany, Boronate Affinity Quenching Technology is based on affinity of boronate for glycated proteins, fluorescent binding and quenching which have measuring range: 4–15% and imprecision: <3%.

Serum and urine samples were analyzed by HumaStar 200 system which is a product of Human Germany, which is an open fully automated chemistry analyzer, awarded the international iF product design award.

4.5.1 Method of analysis:

1. **Cholesterol, Triglycerides**: colorimetric enzymatic test for the quantitative determination in serum sample.

2. **HDL, LDL**: homogeneous enzymatic color assay for the quantitative determination in serum sample.

3. **Alkaline Phosphatase**: enzymatic color test for the quantitative determination in serum sample.

4. **GOT, GPT, Urea**: enzymatic ultraviolet (UV) test for the quantitative determination in serum sample.

5. **Creatinine**: colorimetric test for the quantitative determination in serum sample.

Microalbuminuria: immune turbidimetric test for the quantitative determination in random midstream urine sample.

All kits used are produced by Human Germany according to the recommendations of the used systems. The normal cutoff values for each test were obtained from kits sheets as the following: CHOL ≤ 190 mg/dl. TG ≤ 150. HDL ≥ 60 mg/dl. LDL ≤ 129 mg/dl. ALK PHOS ≤104 U/L,129 U/L for female, male respectively. GOT ≤ 31 U/L, 35 U/L for female, male respectively. GPT ≤ 34 U/L, 45 U/L for female, male respectively. BU ≤ 50 mg/dl. CREAT ≤0.9 mg/dl, 1.1 mg/dl for female, male respectively. MLAB 0-30 mg/l. HbA1c ≤ 7% (NGSP5/DCCT6) for glycemic control. Internal and external controls were used at the start and at the end of each run of samples to maximize the accuracy of results. Internal control by using recommended Human controls kits (Serodos and Serodos Plus for serum tests, Mircoalbumin Standard for urine test and HumaMeter A1c control for HbA1c). External control by comparison of HbA1c results with HPLC method (D10) from BioRad.

4.6 Data analysis

Statistical Product and Service Solutions (SPSS V.22, IBM SPSS statistic) was used for data entry and analysis. Descriptive statistical analysis was used to determine the Mean ± SD (SD., standard deviation) for numerical variables, in addition to the frequency and percentage for categorical variables. Univariate analysis using Chi-square and fisher exact tests were used to examine the association between categorical independent variables

(e.g., socio demographic, medical history, ocular history, laboratory tests) and the dependent variables (NPDR, PDR and Maculopathy). Statistical significance was considered at $P < 0.05$.

Chapter Five

Results

5.1 Prevalence of diabetic retinopathy

Prevalence of diabetic retinopathy (DR) among diabetic patients was found to be 41.8%. While the prevalence of NPDR was 50.3% (Mild NPDR 38.5%, 10.6% for moderate NPDR and 1.2% for severe NPDR), PDR was 9.9% and 39.7% for DME (mild DME was 17.4%, moderate DME 15.5% and severe DME was 6.8%). Prevalence of vision threatening (PDR, DME) was 49.7%. Pie chart (1.1) below shows prevalence and stages of diabetic retinopathy.

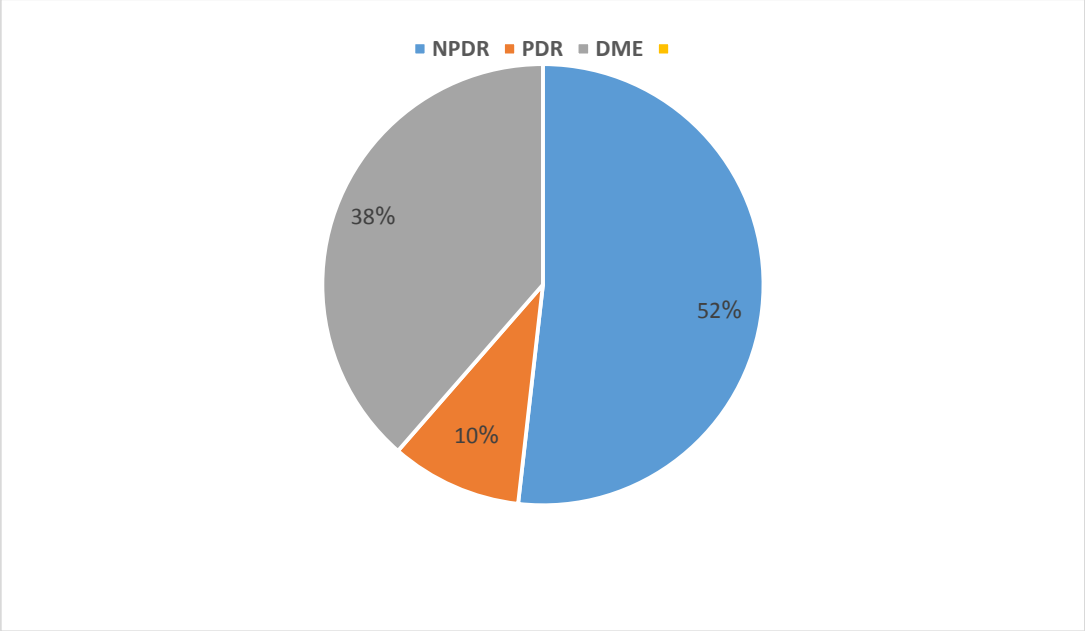

Chart (1.1): Prevalcne of Diabetic retinopathy stages

*NPDR: non- proliferative diabetic retinopathy, * PDR: proliferative diabetic retinopathy *DME: diabetic macular edema.

5.2 Description of characteristics of study participants

5.2.1 Socio-demographic factors of diabetic retinopathy

The mean age of participants was 56.48 ± 12.337 years, the predominant age category was 55-64 with 36.4% of participants. 52.7 % of them were females. 56.1% of participants were from North West Bank. More than half of participants, 51.9% had had primary education.

5.2.2 Medical history

The BMI mean was 30.3349 ± 5.59523, 38.4 % of them were over weighted whereas 49.6% were obese. DM duration mean was 9.69 ± 7.866 years, Type 2 DM was predominant among participants with 92.5% whereas 7.5% of participants had Type 1 DM. 46.2% of participants were treated with oral hypoglycemic agents, 25.5% with insulin and 17.4% with a combination of both oral hypoglycemic agents and insulin. 55.3% had hypertension, 12.7% had a history of systemic steroid therapy. Only 20.5% were current smokers.

5.2.3 Ocular history

10.6% of participants had previous ocular trauma. 6% were previously treated with ocular topical steroid and 14.8% had treatment for retinopathy using various medical and surgical methods.

5.2.4 Laboratory tests

The mean of HbA1c was 8.2229 ± 1.86130 %, 68.1% of participants had non-controlled HbA1c level. The mean of TG was 189.5844 ± 132.33346 mg/dl, 50.1% of them had abnormal TG level. The mean of HDL was 48.6512 ± 14.51382 mg/dl, 83.9% of them had abnormal level. The mean of ALK PHOS was 229.8571 ± 114.79696 U, 93.8% of them had abnormal level. The mean of CREAT was 1.0285 ± 0.47192 mg/dl, 41.0% of them had abnormal level. The mean of BU was 34.2735 ± 18.88311 mg/dl, 12.7% of them had abnormal level. The mean of MLAB was 68.5577 ± 78.17979 mg/dl, with 54.8% had microalbuminuria and only 2.1% had macroalbuminuria.

5.3 Univatiate analysis for Diabetic retinopathy status

5.3.1 Socio-demographic Factors of diabetic retinopathy

Most of DR patients 29 (42.6%) were from the north governorates. (51%) of DR patients were females and about 64 (40%) of patients were in 55-64 age group. 54% of DR patients also had primary education. Table (3) shows Socio-demographic factors of DR patients.

Table (3): Socio-demographic factors of DR patients.

	Absence of DR (1) N(%)	**Presence of DR N(%)**	***P*-value***
Directorates Categories			0.554
North of West Bank	124 (57.4)	92 (42.6)	
Middle of West Bank	37 (54.4)	31 (45.6)	
South of West Bank	63 (62.4)	38 (37.6)	
Sex			0.696
Female	120 (59.1)	83 (40.9)	
Male	104 (57.1)	78 (42.9)	
Age Categories			0.602
≤44 Years	26 (57.8)	19 (42.2)	
45-54 Years	63 (63.0)	37 (37.0)	
55-64 Years	76 (54.3)	64 (45.7)	
≥65	59 (59.0)	41 (41.0)	
Education Level			0.473
Not educated	21 (56.8)	16 (43.2)	
Primary education	112 (56.0)	88 (44.0)	
Secondary education	45 (57.0)	34 (43.0)	
High education	46 (66.7)	23 (33.3)	

1: Diabetic retinopathy * χ^2-test

5.3.2 Medical and Ocular Characteristics of diabetic retinopathy

For medical characteristics, the results showed statistically significant association between DR and BMI (P = .035). Majority of DR patients were obese 80 (41.9%). And 36.5% were overweight. 2 patients only were underweight. 149 of 161 had type 2 diabetes mellitus (41.9%) of all patients. Univariate analysis also showed statistically significant association between DR and DM duration (P = .002)., 94 (57.8%) of patients had duration of DM more than 10 years. Hypertension was found in 86 patients without any statistically significant association. 127 of patients were not smokers, only 22 and 12 of patients took any type of

systemic and ocular steroid respectively. Table (4) showed the medical and ocular characteristics of diabetic patients.

Table (4): Medical and ocular characteristics of DR patients.

	Absence of DR [3] N(%)	**Presence of DR N(%)**	***P*-value***
BMI categories [1] Under weight Normal weight Over weight Obesity	0 (0.0) 19 (43.2) 94 (63.5) 111 (58.1)	2 (100.0) 25 (56.8) 54 (36.5) 80 (41.9)	**0.035**
DM types [2] Type 1 DM Type 2 DM	17 (58.6) 207 (58.1)	12 (41.4) 149 (41.9)	0.960
DM duration categories ≤4 Years 5-9 Years 10-19 Years ≥20 Years	85 (67.5) 52 (66.7) 65 (49.2) 22 (44.9)	41 (32.5) 26 (33.3) 67 (50.8) 27 (55.1)	**0.002**
Hypertension Absent Present	97 (56.4) 127 (59.6)	75 (43.6) 86 (40.4)	0.523
Current Smoking No Yes	179 (58.5) 45 (57.0)	127 (41.5) 34 (43.0)	0.805
Systemic Steroid Therapy No Yes	197 (58.6) 27 (55.1)	139 (41.4) 22 (44.9)	0.640
Ocular trauma No Yes	197 (57.3) 27 (65.9)	147 (42.7) 14 (34.1)	0.292
Topical steroid therapy No Yes	213 (58.8) 11 (47.8)	149 (41.2) 12 (52.2)	0.299
Retinopathy treatment No Yes	197 (60.1) 27 (47.4)	131 (39.9) 30 (52.6)	0.073

1: Body mass index, 2: Diabetes Mellitus, 3: Diabetic retinopathy * χ^2-test.

5.3.3 Laboratory characteristics of diabetic retinopathy

the results showed statistically significant association between DR and LDL (*P* = .034), GOT level (*P* = .016), BU (*P* = .044). 118 (72.7%) of patients had non-controlled HbA1c, 80 patients also had abnormal TG levels. Not as LDL, no statistically significant association between DR and HDL 138 (42.7%) had abnormal HDL levels. For Albuminuria the majority of patients (53.4%) had microabuminuria and only 3 (1.9) patients had macroabuminuria. Table (5) shows the laboratory characteristics of diabetic patients.

Table (5): laboratory characteristics of diabetic retinopathy patients.

	Absence of DR N(%)	**Presence of DR N(%)**	***P*-value***
HbA1c [(1)] Controlled Non-controlled	80 (65.0) 144 (55.0)	43 (35.0) 118 (45.0)	0.062
TG [(2)] Normal Abnormal	111 (57.8) 113 (58.5)	81 (42.2) 80 (41.5)	0.884
CHOL [(3)] Normal Abnormal	136 (57.6) 88 (59.1)	100 (42.4) 61 (40.9)	0.781
HDL [(4)] Normal Abnormal	39 (62.9) 185 (57.3)	23 (37.1) 138 (42.7)	0.411
LDL [(5)] Normal Abnormal	155 (55.0) 69 (67.0)	127 (45.0) 34 (33.0)	**0.034**
ALK PHOS [(6)] Normal Abnormal	16 (66.7) 208 (57.6)	8 (33.3) 153 (42.4)	0.384
GOT [(7)] Normal Abnormal	173 (55.3) 51 (70.8)	140 (44.7) 21 (29.2)	**0.016**
GPT [(8)] Normal Abnormal	206 (57.5) 18 (66.7)	152 (42.5) 9 (33.3)	0.354

CREAT [9] Normal Abnormal	137 (60.4) 87 (55.1)	90 (39.6) 71 (44.9)	0.301
BU [10] Normal Abnormal	202 (60.1) 22 (44.9)	134 (39.9) 27 (55.1)	**0.044**
Albuminuria [11] Normal microalbuminuria Microalbuminuria Macroalbuminuria	 94 (56.6) 125 (59.2) 5 (62.5)	 72 (43.4) 86 (40.8) 3 (37.5)	0.851

1: Glycated Hemoglobin, 2: Triglycerides, 3: Cholesterol, 4: High Density Lipoprotein, 5: Low Density Lipoprotein, 6: Alkaline Phosphatase, 7: Glutamic-Oxaloacetic Transaminase, 8: Glutamic-Pyruvic Transaminase, 9: Creatinine, 10: Blood Urea, 11: Albuminuria. * χ^2-test

5.4 Univariate Analysis for Non-Proliferative Diabetic Retinopathy Stages (NPDR)

5.4.1 Socio-Demographic Factors of NPDR

Majority of NPDR patients were from the north west bank where 37 had mild and 6 patients had moderate NPDR. 31 of males and females had mild NPDR. only 13 of the patients were under age of 40, where total of 31(38.2%) of patients were in age group of (55-64). Table (6) shows the socio-Demographics factors of NPDR stages.

Table (6): Socio-Demographics factors of NPDR stages

Variable	Mild NPDR(1) N(%)	Moderate NPDR N(%)	Severe NPDR N(%)	*P*-value*
Directorates	37 (86.0)	6 (14.0)	0 (0)	0.051
Categories	10 (83.3)	2 (16.7)	0 (0)	
North of West Bank	15 (57.7)	9 (34.6)	2 (7.7)	
Middle of West Bank				
South of West Bank				
Sex	31 (75.6)	8 (19.5)	2 (4.9)	0.359
Female	31 (77.5)	9 (22.5)	0 (0)	
Male				
Age Categories	11 (84.6)	2 (15.4)	0 (0)	0.798
≤44 Years	13 (81.3)	3 (18.8)	0 (0)	
45-54 Years	22 (68.8)	9 (28.1)	1 (3.1)	
55-64 Years	16 (80.0)	3 (15.0)	1 (5.0)	
≥65				
Education Level	9 (81.8)	2 (18.2)	0 (0)	0.720
Not educated	29 (74.4)	8 (20.5)	2 (5.1)	
Primary education	16 (84.2)	3 (15.8)	0 (3.1)	
Secondary education	8 (66.7)	4 (33.3)	0 (0)	
High education				

1: Non-Proliferative diabetic retinopathy * χ^2-test

5.4.2 Medical and Ocular Characteristics of NPDR

Results of Univariate analysis showed statistically significant association between NPDR and DM duration (P = .044), 41(54.3%) of patients had DM more than 10 years. Overweight and obesity found in (23 and 26) of patients respectively. (8.6%) of the patients had DM type 2 and (56.7%) had hypertension majority of them (32) had mild NPDR. Table (7) shows the medical and ocular characteristics of NPDR.

Table (7): Medical and Ocular Characteristics of NPDR stages.

Variable	Mild NPDR N(%)	Moderate NPDR N(%)	Severe NPDR N(%)	*P*-value*
BMI categories [1] Under weight Normal weight Over weight Obesity	1 (100.0) 12 (92.3) 23 (74.2) 26 (72.2)	0 (0) 1 (7.7) 7 (22.6) 9 (25.0)	0 (0) 0 (0) 1 (3.3) 1 (2.8)	0.851
DM types [2] Type 1 DM Type 2 DM	6 (85.7) 56 (75.7)	1 (14.3) 16 (21.6)	0 (0) 2 (2.7)	0.804
DM duration categories ≤4 Years 5-9 Years 10-19 Years ≥20 Years	18 (85.7) 16 (100.0) 18 (58) 10 (67.9)	3 (14.3) 0 (0) 11 (35.5) 3(23.1)	0 (0) 0 (0) 2 (6.5) 0 (0)	**0.044**
Hypertension Absent Present	30 (85.7) 32 (69.6)	5 (14.3) 12 (26.1)	0 (0) 2 (4.3)	0.172
Current Smoking No Yes	45 (74.0) 17(81.0)	13 (22.7) 4 (19.0)	2 (3.3) 0(0)	0.158
Systemic Steroid Therapy No Yes	65 (75.0) 6 (100.0)	13 (21.7) 0 (19.0)	2 (2.7) 0(0)	0.370
Ocular trauma No Yes	55 (76.4) 7(77.8)	15 (20.8) 2 (22.2)	2 (2.8) 0(0)	0.700
Topical steroid therapy No Yes	55 (76.4) 7(77.8)	15 (20.8) 2 (22.2)	2 (2.8) 0(0)	0.263
Retinopathy treatment No Yes	56 (77.8) 6(66.7)	15 (20.8) 2 (22.2)	1 (1.4) 1(11.1)	0.202

1: Body mass index, 2: Diabetes Mellitus, * χ^2-test

5.4.3 Laboratory Characteristics of NPDR

The Results showed statistically significant association between NPDR and BU (*P* = .047), (80.9%) of mild NPDR patients had normal levels of BU and only 6 (46.2%) of severe NPDR had normal levels of BU. For non-controlled HbA1c there were 44 of mild NPDR patients. Majority of mild NPDR patients also had abnormal levels of HDL, while (73%) of them had normal levels of LDL. Table (8) below shows laboratory characteristics of NPDR Stages.

Table (8): laboratory characteristics of NPDR Stages

Variable	Mild NPDR N(%)	Moderate NPDR N(%)	Severe NPDR N(%)	*P*-value*
HbA1c [(1)] Controlled Non-controlled	18(81.8) 44(74.6)	4 (18.2) 13 (22.0)	0 (0) 2(3.4)	0.616
TG [(2)] Normal Abnormal	32(84.2) 30(69.8)	6 (15.8) 11 (25.6)	0 (0) 2(2.5)	0.198
CHOL [(3)] Normal Abnormal	41(71.9) 21(87.5)	15 (26.3) 2 (8.3)	1 (1.8) 1(4.2)	0.171
HDL [(4)] Normal Abnormal	10(90.9) 52(74.3)	1 (9.1) 16 (22.9)	0 (0) 2(2.9)	0.469
LDL [(5)] Normal Abnormal	50(73.5) 12(92.3)	17 (25.0) 0 (0)	1 (1.5) 1(7.7)	0.065
ALK PHOS [(6)] Normal Abnormal	1(50.0) 61(77.2)	1 (50.0) 16 (20.3)	0 (0) 2(2.5)	0.588
GOT [(7)] Normal Abnormal	51(73.9) 11(91.7)	16 (23.2) 1 (8.3)	2 (2.9) 0 (0)	0.398
GPT [(8)] Normal Abnormal	56(75.7) 6 (85.7)	16 (21.6) 1 (14.3)	2 (2.7) 0 (0)	0.804
CREAT [(9)] Normal Abnormal	32(76.2) 30 (76.9)	8 (19.0) 9 (23.1)	2 (4.8) 0 (0)	0.365

BU [10] Normal Abnormal	55(80.9) 7 (53.8)	11 (16.2) 6 (46.2)	2 (2.9) 0 (0)	**0.047**
Albuminuria [11] Normal.microalbuminuria Microalbuminuria Macroalbuminuria	31(81.6) 30 (71.4) 1 (100.0)	6 (15.8) 11 (26.2) 0 (0)	1 (2.6) 1 (2.4) 0 (0)	0.807

1: Glycated Hemoglobin, 2: Triglycerides, 3: Cholesterol, 4: High Density Lipoprotein, 5: Low Density Lipoprotein, 6: Alkaline Phosphatase, 7: Glutamic-Oxaloacetic Transaminase, 8: Glutamic-Pyruvic Transaminase, 9: Creatinine, 10: Blood Urea, 11: Albuminuria. * χ^2-test.

5.5 Univariate Analysis for NPDR and Vision threatening (PDR, DME)

5.5.1 Socio-Demographic Factors of NPDR & Vision threatening.

Chi-square testing showed statistically significant association between NPDR and vision threatening with Directorates (P = .028). 43 (46.7%) and 49 (53.3%) of patients were form north governorates for both NPDR and vision threatening respectively. (51.6%) of patients with vision threatening were females. Only 19 of DR patients were under age of 40 years. for age group between 55-64 Years there were 32 patients of NPDR and vision threatening and Majority of patients had primary education. Table (9) shows socio-demographic factors of NPDR and vision threatening patients.

Table (9): socio-demographic factors of NPDR and vision threatening patients.

Variable	NPDR N(%)	Vision Threatening (PDR,DME) N(%)	*P*-value*
Directorates Categories North of West Bank Middle of West Bank South of West Bank	43 (46.7) 12 (38.7) 26 (68.4)	49 (53.3) 19 (61.3) 12 (31.6)	**0.028**
Sex Female Male	41 (49.4) 40 (51.3)	42 (51.6) 38 (48.7)	0.811
Age Categories ≤44 Years 45-54 Years 55-64 Years ≥65	13 (68.4) 16 (43.2) 32 (50.0) 20 (48.8)	6 (31.6) 21 (56.6) 32 (50.0) 21 (51.2)	0.351
Education Level Not educated Primary education Secondary education High education	11 (64.7) 39 (44.8) 19 (55.9) 12 (52.2)	6 (35.3) 48 (55.2) 15 (44.1) 11 (47.8)	0.406

- χ^2-test

5.5.2 Medical and Ocular Characteristics of NPDR & Vision threatening

Univariate analysis showed statistically significant association between NPD, vision threatening and systemic steroid therapy (P = .020), retinopathy treatment (P = .016). Obesity were found in 34 of patients with vision threatening and (50.3%) of these patients had type 2 DM. about (58%) of all patients had DM more than 10 years.

14 patients only of all patients had exposed to any type of ocular trauma. Univariate analysis did not show any statistically association between smoking and NPDR and Vision threatening. Table (10) shows medical and ocular Characteristics of NPDR and vision threatening patients.

Table (10): Medical and ocular Characteristics of NPDR and vision threatening patients.

Variable	NPDR N(%)	Vision Threatening (PDR,DME) N(%)	*P*-value*
BMI categories [(1)] Under weight Normal weight Over weight Obesity	1 (50.0) 13 (52.0) 31 (56.4) 36 (45.6)	1 (50.0) 12 (48.0) 24 (43.6) 43 (54.4)	0.672
DM types [(2)] Type 1 DM Type 2 DM	7 (58.3) 74 (49.7)	5 (41.7) 75 (50.3)	0.563
DM duration categories ≤4 Years 5-9 Years 10-19 Years ≥20 Years	21 (51.2) 16 (59.3) 31 (47.0) 13 (48.1)	20 (48.8) 11 (40.7) 35 (53.0) 14 (51.9)	0.747
Hypertension Absent Present	35 (47.3) 46 (52.9)	39 (52.7) 41 (47.1)	0.481
Current Smoking No Yes	60 (47.2) 21 (61.8)	67 (52.8) 13 (38.2)	0.133
Systemic Steroid Therapy No Yes	75 (54.0) 6 (27.3)	64 (46.0) 16 (72.7)	**0.020**
Ocular trauma No Yes	72 (49.0) 9 (64.3)	75 (51.0) 5 (35.7)	.274
Topical steroid therapy No Yes	75 (50.3) 6 (50.0)	74 (49.7) 6 (50.0)	.928

1: Body mass index, 2: Diabetes Mellitus, * χ^2-test

5.5.3 Laboratory characteristics of NPDR & Vision threatening

No any statistically significant association between NPD, vision threatening and laboratory findings were found. Only 8 (0.04%) patients of NPDR and vision threatening had normal levels of alkaline phosphatase. Also (8%) and (12%) of all patients had abnormal levels of GPT and GOT respectively. For more information, table (11) shows laboratory characteristics of NPDR and vision threatening.

Table (11): laboratory characteristics and vision threatening patients.

Variable	NPDR N(%)	Vision Threatening (PDR,DME) N(%)	*P*-value*
HbA1c [(1)] Controlled Non-controlled	22 (50) 59 (50.4)	22 (50) 58 (49.6)	0.876
TG [(2)] Normal Abnormal	38 (46.9) 43 (53.8)	43 (53.1) 37 (46.3)	0.432
CHOL [(3)] Normal Abnormal	22 (50) 59 (50.4)	22 (50) 58 (49.6)	0.051
HDL [(4)] Normal Abnormal	11 (47.8) 70 (50.7)	12 (52.2) 68 (49.3)	0.825
LDL [(5)] Normal Abnormal	68 (53.1) 13 (39.4)	60 (46.9) 20 (60.6)	0.176
ALK PHOS [(6)] Normal Abnormal	2 (25) 79 (51.6)	6 (75) 74 (48.4)	0.167
GOT [(7)] Normal Abnormal	69 (48.9) 12 (60)	72 (51.1) 8(40)	0.474
GPT [(8)] Normal Abnormal	74 (48.7) 7 (77.8)	78 (51.3) 8 (22.2)	0.167

CREAT [9] Normal Abnormal	42 (46.7) 39 (54.9)	48 (53.3) 32 (54.1)	0.342
BU [10] Normal Abnormal	68 (50.4) 13 (50)	67 (49.6) 13 (50)	0.972
Albuminuria [11] Normal.microalbuminuria Microalbuminuria Macroalbuminuria	38 (52.8) 42 (48.8) 1 (33.3)	34 (47.2) 44 (51.2) 2 (66.7)	0.742

1: Glycated Hemoglobin, 2: Triglycerides, 3: Cholesterol, 4: High Density Lipoprotein, 5: Low Density Lipoprotein, 6: Alkaline Phosphatase, 7: Glutamic-Oxaloacetic Transaminase, 8: Glutamic-Pyruvic Transaminase, 9: Creatinine, 10: Blood Urea, 11: Albuminuria. * χ^2-test

5.6 Multivariate logistic regression for factors associated with diabetic retinopathy.

Multivariate logistic regression was used to evaluate variables associated with Diabetic retinopathy (DR). While controlling for possible confounding variables (DM duration, retinopathy treatment, HbA1c, LDL, GOT and BU) in calculating the adjusted odds ratio (aOR). Variables included in the model were only those with a significant level <0.05 in the univariate analysis. After applying binary logistic regression model on each factors associated with DR, (10-19) DM duration ($P < 0.05$), abnormal levels of LDL ($P = 0.008$), abnormal levels of GOT ($P < 0.05$), and Overweight ($P < 0.05$) were still to be statistically significant with DR and the rest were not statistically significant. Patients who had DM for (10-19) years were more likely to have DR (aOR 1.843, 95%CI 1.05-3.22), although DM duration more than 20 years (aOR 2.005,95%CI 0.91-4.40) was associated with increased odds of DR, they were not statistically significant. Patients with abnormal level of LDL (aOR 0.50, 95%CI 0.30-0.83), GOT

(aOR 0.49,95% CI 0.27-0.89) and overweight patients (aOR 0.39, 95%CI 0.19-0.80) were less likely to develop DR (protective factor).

Table (12): shows multivariate logistic regression for factors associated with diabetic retinopathy.

Variables	aOR[(1)]	95%CI[(2)]	P-value
DM duration			
5-9 Years	1.034	0.55-1.931	0.917
10-19 Years	1.843	1.054-3.220	**0.032**
≥20 Years	2.005	0.913-4.403	0.083
≤4 Years±			
Retinopathy treatment			
Yes	1.119	0.583-2.148	0.736
No*			
HbA1c[(3)]			
Non-controlled	1.416	0.866-2.316	0.166
Controlled ^			
LDL[(4)]			
Abnormal	0.501	0.301-0.835	**0.008**
Normalγ			
GOT[(5)]			
Abnormal	0.494	0.274-0.890	**0.019**
Normal&			
BU[(6)]			
Abnormal	1.709	0.897-3.254	0.103
Normalω			
BMI[(7)]			
Over weight	0.393	0.193-0.801	**0.010**
Obesity	0.572	0.285-1.148	0.116
Normal weight#			

1: Adjusted Odds Ratio, 2:confidence intervals 95% , 3: Glycated Hemoglobin, 4: Low Density Lipoprotein, 5: Glutamic-Oxaloacetic Transaminase, 6: Blood Urea, 7: Body Mass Index, ±:≤4 Years Reference category (aOR=1), *: No diabetic retinopathy treatment Reference category (aOR=1),^: controlled HbA1c Reference category (aOR=1), γ: Normal LDL levels Reference category (aOR=1), &: Normal GOT levels Reference category (aOR=1), ω: Normal BU levels Reference category (aOR=1), #: Normal Weight of BMI Reference category (aOR=1).

5.7 Multivariate logistic regression for factors associated with NPDR and Vision threatening levels (PDR, DME).

After applying binary logistic regression model on each factors associated with NPDR and Vision threatening, we found that systemic steroid therapy ($P < 0.05$) and CHOL Levels ($P = 0.043$) were significantly associated with vision threating (PDR, DME). Our findings found that Patients who had systemic steroid therapy (aOR 2.94, 95%CI 1.05-8.02), and abnormal levels of CHOL (aOR 2.94, 95%CI 1.05-8.02) have a higher risk to develop vision threating.

Table (13): shows multivariate logistic regression for factors associated with NPDR and Vision threating (PDR, DME).

Variables	aOR(1)	95%CI(2)	P-value
Directorates Categories			
Middle of West Bank	1.255	0.531-2.965	0.605
South of West Bank	0.459	0.202-1.044	0.063
North of the West Bank^			
Systemic Steroid Therapy			
Yes	2.948	1.059-8.209	**0.039**
No*			
CHOL(3)			
Normal	2.002	1.021-3.926	**0.043**
Abnormal #			

1: Adjusted Odds Ratio, 2: confidence intervals 95% , 3: Cholesterol levels, ^: North west bank directorates Reference category (aOR=1), *:No seriod therapy Reference category (aOR=1), #: Abnormal levels of CHOL Reference category (aOR=1).

Chapter Six
Discussion

The aim of this study was to assess the prevalence of Diabetic retinopathy and identify its mostly associated factors among the Palestinian DM patients in the West Bank directorates. In this chapter we will discuss the prevalence of DR, stages, associated risk factors and strength and limitations and recommendations of the study.

6.1 Prevalence of diabetic retinopathy

Results showed that prevalence of any diabetic retinopathy among Palestinians was (41.8%). This prevalence considered higher than global prevalence which was (34.6%) (Joanne et al., 2009).

The prevalence also was higher than some studies that conducted in USA, UK France and South Korea which were (28.5%), (22.5%), (32.2%) and (18%) respectively (Xinzhi et al., 2012; Martin et al., 2014; Massin P et al., 2009; Ji-Hyun et al.,2008). It was lower than Malaysia and India which were (51.6%) and (66.2%) respectively (Tajunisah et al., 2015).

In the Middle East, based on the study we conducted, Palestine occupied the fourth rank in the prevalence of DR, after Oman (66.4%), Jordan (64%) and Yemen (55%) (El Haddad et al., 2012; Maha titi et al.,2013; Mahfouth et al.,2009).

DR Prevalence widely varied between studies conducted among different populations. This might be due to differences in the characteristics of each

study population and the used methods and criteria for assessing the presence of DR. Based on the previous results, the prevalence of DR in Palestine considered to be high compared to other countries. This may be due to poor glycemic control in Palestine (Abu-Al Halaweh et al., 2017).

Prevalence of DR showed that less than other diabetic complications among Palestinians. Prevalence of neuropathy and nephropathy were (98.5%) and (66.2%) respectively according to WHO report (WHO, 2015).

6.2 Prevalence of diabetic retinopathy stages

The study has found that the prevalence of diabetic retinopathy stages was for NPDR 50.3% (Mild NPDR 38.5%, 10.6% for moderate NPDR and 1.2% for severe NPDR), PDR was 9.9% and 39.7% for DME (mild DME was 17.4%, moderate DME 15.5% and severe DME was 6.8%). Prevalence of vision threatening (VTDR) was 49.7%.

Vision threatening (VTDR) which is the stage where the vision loss occurs. Our study showed high prevalence of VTDR Relative to global prevalence which is (25.3%).

This might be due to poor glycemic and lipid control among diabetic patients and lack of medical follow up of patients (Abu-Al Halaweh et al., 2017).

6.3 Major of diabetic retinopathy associated factors

For all DR, the most associated factors were BMI, GOT, LDL, duration of DM and BU which supports the results of a previous study conducted in Heidelberg -Germany. The same previous study contradicts our study in that HbA1c and age were found to be a significant factor, while it was not in this one (Peter et al., 2014).

BMI is considered one of the most associated factors of DR. Meta-analysis of global DR showed that BMI in correlation with HbA1c, cholesterol and hypertension appears to be associated with the progression of DR in type 2 diabetes and may serve as a predictive factor for the development of this important cause of visual loss in developing countries (Joanne et al, 2009). Although the underlying pathophysiological mechanisms supporting the association between higher BMI and DR are yet to be defined, several biological theories have been proposed including the potential involvement of platelet function, blood viscosity, aldose reductase activity, and vasoproliferative parameters such as vascular endothelial growth factor (VEGF). Furthermore, the concentration of VEGF has been found to be higher in the vitreous of eyes with PDR.

An important note was that GOT, which was significant factor for DR in our study, was not considered to be an independent variable on any previous study that we know of. This requires further researches and study to clarify the relationship between DR and GOT. The lack of previous

studies on this subject prompted us to examine the relationship between DR and GOT.

There were several studies conducted to determine relation between LDL levels and DR. one of the most important studies was conducted in UK by Klein R et al., Contrary to our study, this study did not provide evidence for a relationship between increasing levels of LDL and the incidence DR or the worsening of diabetic retinopathy in persons with type 1 and 2 diabetes (Klein et al., 2011). Another study was conducted in China by X Chen et al., this study also has found that there is no any relationship between DR and LDL level, note that this study found a significant association between DR and HDL. On the other hand, several studies found relationship between DR and LDL. One of the most important studies was conducted in among Korean Population by Ji-Hyun et al., like our study, found significant association between LDL and DR, NPDR in particular (Ji-Hyun et al., 2008). Similar to our study, results of Shandong-China Study showed that LDL associated with DME, and VTDR (Zahoe et al., 2015).

Although the Association between LDL and DM is clear, the relation between DR and LDL still unclear. Some researchers suggested that high LDL level promote DM itself, this leads to increase risk of diabetic complications such nephropathy and retinopathy (Omari et al., 2017).

Our research also found significant association between DR and duration of DM. Similar to our study, global prevalence of DR study, for example, found strong relationship between diabetes duration and all DR (Joanne et

al, 2009). Moreover, a meta-analysis study conducted in Africa collected 62 studies from 21 African countries by Burgess P.I et al., results of this study has found significant association between all DR stages and DM duration (Burgess et al., 2012). Early treatment of diabetic retinopathy study (ETDRS) showed that duration of diabetes is probably the strongest predictor for development and progression of retinopathy. Among younger-onset patients with diabetes in the ETDRS, the prevalence of any retinopathy was 8% at 3 years, 25% at 5 years, 60% at 10 years, and 80% at 15 years. Based on previous studies, duration of diabetes considered one of the most important factors of DR as our study found also (ETDRS, 2014).

Blood Urea (BU) also one of associated factors of DR as our study found. In people with Type 2 diabetes and overt kidney disease, 20% progress to kidney failure in 20 years (ETDRS, 2014). Several epidemiological studies were conducted to study the association between BU and DR.

A study was conducted in Heiwzaho-China, has found that BU associated with DR (OR :1.012). Norway study by Mikel H et al. also found the same OR between DR and BU. Unlike our study, Jordanian hospital study was conducted in Amman found no association between DR and BU (Maha titi et al., 2014).

Other studies found that Age, DM type, hypertension, systemic steroid therapy, HbA1c, retinopathy treatment, CREAT and ALK PHOS were associated with all DR, these factors were not associated in our study.

Results of Univariate analysis also showed statistically significant association between NPDR and DM duration. Several studies approved that DM duration associated strongly with NPDR, Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) approved that DM duration associated strongly with NPDR and progression of PDR also (WESDR ,2015). On the other hand, Hans-Peter Hammes et al. through a study conducted in Germany stated that DM duration associated with DME and VTDR rather than NPDR (Peter et al., 2014). We found also significant association between NPDR and BU, Other studies also have supported this relationship, A Kuwaiti study has found that NPDR and PDR significantly associated with BU (Afaf et al., 2007) but that study also concluded that HbA1c is significantly associated to NPDR, in contrast to our study. However, we did not find any other association between NPDR and other DR factors such as HbA1c, LDL, HDL and GOT.

Our results of Chi-square testing also found association between systemic steroid therapy and NPDR and VTDR. Although some studies have shown efficancy of systemic steroid in DME treatment (Gopal Lingam et al.,2013). Some studies also found significant association between DR and systemic steroid therapy. A study conducted in UK found that systemic steroid therapy was a risk factor of NPDR and PDR (Kenan et al., 2013).

In our understanding, we think that the differences between the results of our study and previous studies might be due to the genetic variations among each study population, study design, participant's recruitment

methods (Random, specialized diabetic centers, Ophthalmology departments), different models used for data analysis.

6.4 Strength and limitations

The main strength of this study is that it was the first study of diabetic retinopathy among diabetic patients in whole of the West Bank. Additionally, the study population represented the majority of DM patients in West Bank as the PHC centers of MoH are considered to be the main health care providers (MoH, 2017). Study participants were recruited from all directorates of West Bank.

Another strength was that the detailed slit-lamp examination of all participants was done by the same ophthalmologist. In addition, our study did not depend on previous laboratory tests for patients unlike other previous studies. Also all laboratory tests were done in the same lab by using one standard analyzer.

On the other hand, this study has many limitations, the first one is that medical and ocular history where taken from participants only by face to face interview without returning to the medical archive. The absence of baseline history of retinopathy among participants prior to being diagnosed with DM, could have an important effect on the study results regarding the relation between retinopathy formation and DM.

6.5 Conclusion

Earlier diagnosis of diabetes and diabetic retinopathy (DR) would help to control and prevent DR complications. Population-based education programs and continuous medical evaluation can also improve the health status associated with diabetes and diabetic retinopathy (DR) and improve self-management and prevent eye complications.

6.6 Recommendations

1. Patients with Type 1 and Type 2 diabetes should have annual screening and evaluation for diabetic retinopathy normally after 5 years of diabetes onset.

2. Maintaining near-normal glucose levels (HbA1c), LDL, GOT and BU lowers the risk of retinopathy developing and lowers vision threatening of diabetic retinopathy (VTDR).

3. Referral to an ophthalmologist is necessary if there are any stages of diabetic retinopathy (NPDR, PDR and DME) especially patients with vision threatening VTDR (PDR, DME).

4. We recommend also further studies in Palestine with a larger sample size and another study design such as Cohort study for more representative results.

References

1. Abcouwer SF, Gardner TW. **Diabetic retinopathy: loss of neuroretinal adaptation to the diabetic metabolic environment**. Ann N Y Acad Sci. 2014; 1311:174–190.

2. Abu-Al Halaweh. **Prevalence of diabetes in and associated factors in Palestine**. 2017;96(9):1168–12.

3. Ataur Rahman Khan, Thompson JR, Rosenthal AR. **The prevalence of retinopathy in the insulin-requiring diabetic patients of an English town**. Eye. 1988; 2:424–430.

4. Al-Adsani AM. ***Risk factors for diabetic retinopathy in Kuwaiti type 2 diabetic patients***. **Saudi Med J**.2007; 28:579–83.

5. Al Ghamdi AH, Rabiu M, Hajar S, Yorston D, Kuper H, Polack S. ***Rapid assessment of avoidable blindness and diabetic retinopathy in Taif, Saudi Arabia***. **Br J Ophthalmol**. 2012; 96:1168–72.

6. **Early Treatment Diabetic Retinopathy Study Research Group**. **Fundus photographic risk factors for progression of diabetic retinopathy**. ETDRS report number 12. Ophthalmology. 2016; 98: 823–833.

7. **Early Treatment Diabetic Retinopathy Study Design and Baseline Patient Characteristics Ophthalmology**, Volume 98, Issue 5, 741 – 756.

8. El Haddad OA, Saad MK: ***Prevalence and risk factors for diabetic retinopathy among Omani diabetics***. **Br J Ophthalmol** 1998, 82 (8) :901-6.

9. Fatma Al-Maskari, Sivasubramaniam S, Murthy GV, Gilbert C, Abubakar T, Ezelum C, et al. **Nigeria National Blindness and Visual Impairment Study Group. Causes of blindness and visual impairment in Nigeria: the Nigeria national blindness and visual impairment survey.** Invest Ophthalmol Vis Sci. 2009; 50:4114–4120.

10. Fenwick E. K, Dembele M, Cisse A, Alwata F, AhmedouOuld MY, Coulibaly T, et al. **Diabetic hand infections in hospital practice in Bamako, Mali**. Diabetes Metab. 2006; 32:89.

11. Giani G, Janka HU, Hauner H, Standl E, Schiel R, Neu , A **Epidemiologie und Verlauf des Diabetes mellitus in Deutschland.** Evidenzbasierte Leitlinie DDG-Aktualisierung. 2004; 5:1–12.

12. Gill GV, Huddle KR, Krige LP. ***Intensive health screening of young black diabetics***. **S Afr Med J**.1984; 65:815–816.

13. Hagg S, Thorn LM ,Garg SK, Jackson WE, et al. **Blood pressure and retinopathy in type 1 diabetes**. Ophthalmology. 1990; 97:155–159.

14. Hagg S, Thorn LM, Putaala J, Liebkind R, Harjutsalo V, Forsblom CM, et al. **Incidence of stroke according to presence of diabetic nephropathy and severe diabetic retinopathy in patients with type 1 diabetes**. Diabetes Care. 2013;36(12):4140–6. doi: 10.2337/dc13-0669.

15. Harris MI, Klein R, Cowie CC, Rowland M, Byrd-Holt DD. **Is the risk of diabetic retinopathy greater in non-Hispanic blacks and Mexican Americans than in non-Hispanic whites with type 2 diabetes? a US population study.** Diabetes Care. 2011;21(8):1230–1235.

16. Juan Wang, Aubert RE, Engelgau MM, Thompson TJ, Ali MA, Sous ES, Hegazy M, BadranA: **Diabetes mellitus in Egypt: glycaemic control and microvascular and neuropathic complications**. Diabet Med 1998, 15(12):1045-51.

17. Jenkins, A. J., Joglekar, M. V., Hardikar, A. A., Keech, A. C., O'Neal, D. N., & Januszewski, A. S. (2015). **Biomarkers in Diabetic Retinopathy**. The Review of Diabetic Studies : RDS, 12(1-2), 159–195.

18. Katibeh, M., Pakravan, M., Yaseri, M., Pakbin, M., & Soleimanizad, R. (2015). **Prevalence and Causes of Visual Impairment and Blindness in Central Iran**; The Yazd Eye Study.

19. Kawasaki R, Tanaka S, Tanaka S, Abe S, Sone H, Yokote K, et al. **Risk of cardiovascular diseases is increased even with mild diabetic retinopathy: the Japan Diabetes Complications Study**. Ophthalmology.2013;120(3):574–82.

20. Klein BEK, Moss SE, Klein R, Surawics TS. **The Wisconsin epidemiology study of diabetic retinopathy XIII. Relationship of serum cholesterol to retinopathy and hard exudates**. Ophthalmology.1991;98:1261–1265.

21. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. **The Wisconsin epidemiologic study of diabetic retinopathy. II. Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years**. Arch Ophthalmol. 1984; 102:520–6.

22. Kristin M. Hirahatake; Joanne L. Slavin; Kevin C. Maki; Sean H. Adams; **Associations between dairy foods, diabetes, and metabolic health: Potential mechanisms and future directions**; Metabolism: Clinical and Experimental. 2014;63(5):618-627.

23. Mihardja, L., Soetrisno, U., & Soegondo, S. (2014). ***Prevalence and clinical profile of diabetes mellitus in productive aged urban Indonesians.*** **Journal of Diabetes Investigation**, 5(5), 507–512.

24. Rayn lee, Wong TY. **Diabetic retinopathy and systemic vascular complications**. Prog Retin Eye Res. 2008;27(2):161–176.

25. Rugayah B. **Diabetes mellitus among adults 30 years and above** - National Health and Morbidity Survey 1996-1997.

26. Sadiq S, Chatterjee A, Vernon S. **Progression of diabetic retinopathy and rubeotic glaucoma following cataract surgery**. *Eye*. 1995.

27. Schmidt, K.-G., Bergert, H., & Funk, R. H. . (2008). **Neurodegenerative Diseases of the Retina and Potential for Protection and Recovery**. Current Neuropharmacology, 6(2), 164–178.

28. Shriwas SR, Rabiu M, Hajar S, Yorston D, Kuper H, Polack S. ***Rapid assessment of avoidable blindness and diabetic retinopathy in Taif, Saudi Arabia***. **Br J Ophthalmol**. 2012;96(9):1168–72.

29. Shriwas SR, Rahman Isa AB, Reddy SC, Mohammad M,Mohammad WBW, Mazlan M. ***Risk factors for Retinopathy in Diabetes Mellitus in Kelantan, Malaysia***. **Med. J. Malaysia** 1996; 51: 447-52.

30. Tajunisah J, Wang F, Ji LN: ***Risk Factors of Diabetic retinopathy in type 2 diabetic patients.*** **Chin Med J (Engl)** 119(10):822-6. 2006 May 20.

31. The Diabetes Control and Complications Trial Research Group. ***The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus***. **N Engl J Med**. 1993;329(14):977–986.

32. UK Prospective Diabetes Study Group. ***Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes***: UKPDS 38**. BMJ**. 1998;317(7160):703–713.

33. Wu L, Fernandez-Loaiza P, Sauma J, Hernandez-Bogantes E, Masis M. ***Classification of diabetic retinopathy and diabetic macular edema.*** **World Journal of Diabetes**. 2013;4(6):290-294. doi:10.4239/wjd.v4.i6.290.

34. Xie J., Fenwick E. K., Taouk Y., et al. ***Relative importance and contribiton of risk factors for diabetic retinopathy and macular edema***. **Journal of Diabetes & Metabolism**. 2014;5, article 337 doi: 10.4172/2155-6156.1000337.

35. Yau, J. W. Y., Rogers, S. L., Kawasaki, R., Lamoureux, E. L., Kowalski, J. W., Bek, T., … **for the Meta-Analysis for Eye Disease (META-EYE) Study Group. (2012).** Global Prevalence and Major Risk Factors of Diabetic Retinopathy. Diabetes Care, 35(3), 556–564.

36. Zhang, X., Chee, W. K., Liu, S., Tavintharan, S., Sum, C. F., Lim, S. C., & Kumari, N. (2018). **Association of plasma osteopontin with diabetic retinopathy in Asians with type 2 diabetes**. Molecular Vision, 24, 165–173.

Appendices

Appendix 1

Study consent form

<u>موافقة على الاشتراك في دراسية علمية</u>

يقوم مجموعة من طلبة كلية الطب وعلوم الصحة في جامعة النجاح الوطنية بدراسة لبحث العلاقة بين مرض السكري وتأثيراته على العين.

يهدف هذا البحث إلى إيجاد نسبة انتشار مشاكل العيون عند الأشخاص المصابين بمرض السكري إضافة الى إيجاد علاقة مع مجموعة من عوامل الخطورة التي تزيد نسبة التعرض لمشاكل العين المرتبطة بالسكري.

الرجاء أن تأخذ(ي) الوقت الكافي لقراءة المعلومات التالية بتأنّي قبل أن تقرر(ي) إذا كنت تريد(ين) الاشتراك في الدراسة العلمية، بإمكانك طلب إيضاحات أو معلومات إضافية عن أي شيء مذكور في هذه الاستمارة أو عن هذه الدراسة ككل.

– من أجل اجراء الفحص الكامل للعيون يجب وضع قطرة موسعة للبؤبؤ في العين، والتي من شأنها أن تسبب مؤقتا غباش في الرؤية وزيادة حساسية العين للضوء الساطع وصداع ولكن بمجرد انتهاء فعالية القطرة على توسيع البؤبؤ تعود الأمور إلى طبيعتها، كما من الممكن أن تؤدي القطرة الى احمرار الوجه وظهور علامات جلدية وزيادة الاحساس بالعطش وجفاف الفم ولكن هذه الاعراض الجانبية تحدث في حالات قليلة ممن يخضعون لهذه القطرة وسيتم فحص العين للتأكد من عدم حدوث أي اعراض جانبية.

– من أجل الاشتراك بالبحث سيتم أخذ عينة دم وبول من المريض من اجل اجراء فحوصات مخبرية لتقيم الوضع الصحي، وسيتم التخلص من العينات حسب البروتوكول المعمول به.
– في حال وافقت/ي على الاشتراك في هذه الدراسة سيبقى اسم حضرتك طي الكتمان.

ولن يكون لأي شخص، ما لم ينص القانون على ذلك، حق الاطلاع على نتيجة البحث المتعلقة بك شخصيا.

لقد شرحت بالتفصيل طبيعة البحث ومجرياته وتأثيراته السلبية. ولقد أجبت على كل أسئلته بوضوح على خير ما أستطيع. وسوف أعلم المشترك بأي تغييرات في مجريات هذا البحث أو تأثيراته السلبية أو فوائده في حال حصولها أثناء البحث.

مع العلم أن هذه الاستمارة تضمن وتحفظ حقوق فريق البحث باشراف الدكتور حمزة الزبدي.

اسم المشترك: _____ رقم الهاتف: _____

التوقيع: _____

Appendix 2

ETDRS Questionnaire

Code:_____

Sex: Male Female

Age:_____

Height:_____ Weigh:_____

Education Level: Non Primary (1-10) Secondary (11-12) High (University)

Type of DM: T1 T2 Unknown

Duration of DM:_____

Current treatment of DM (you can chose more than one):

Diet Oral hypoglycemic agent Insulin

Hypertension: No Yes ***Current smoker:** No Yes

***Current smoker**: a person who currently either smokes more than one cigarette per day or one cigar per week or chews 30 g of tobacco per month, for at least one year.

Systemic Steroid Therapy: Yes No If **Yes, Duration: _ Dose:_____**

Ophthalmic History:

	OD (Right)	**OS (Left)**
Ocular Trauma	**No Physical Chemical**	**No Physical Chemical**
Topical Steroid Therapy	**No Yes** If Yes, Medication:_____ Duration:_____	**No Yes** If Yes, Medication:_____ Duration:_____
Retinopathy Therapy	**No Yes** If Yes, circle the type (you can chose more than one) **Injections Laser Surgery**	**No Yes** If Yes, circle the type (you can chose more than one) **Injections Laser Surgery**
Glaucoma Therapy	**No Yes**	**No Yes**

	OD (Right)							**OS (Left)**						
IOP														
C/D ratio														
PEX														
Retinopathy	No Mild NPDR Moderate NPDR Severe NPDR PDR Mild CME Moderate CME Severe CME							No Mild NPDR Moderate NPDR Severe NPDR PDR Mild CME Moderate CME Severe CME						
Pterygium														
Cataract	**Previous Surgery**							**Previous Surgery**						
	Nuclear (O/C)	1	2	3	4	5	6	**Nuclear (O/C)**	1	2	3	4	5	6
		1	2	3	4	5	6		1	2	3	4	5	6
	Cortical	1	2	3	4	5		**Cortical**	1	2	3	4	5	
	Posterior Subcapsular	1	2	3	4	5		**Posterior Subcapsular**	1	2	3	4	5	

جامعة النجاح الوطنية

كلية الدراسات العليا

نسبة انتشار اعتلال الشبكية السكري والعوامل المرتبطة به بين مرضى السكري في الضفة الغربية: دراسة مقطعية

إعداد

ابراهيم عبدالله طه

إشراف

د.حمزة الزبدي

قدمت هذه الأطروحة استكمالاً لمتطلبات الحصول على درجة الماجستير في برنامج الصحة العامة، بكلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس- فلسطين.

2018

نسبة انتشار اعتلال الشبكية السكري والعوامل المرتبطة به بين مرضى السكري في الضفة الغربية: دراسة مقطعية

اعداد

ابراهيم عبد الله طه

باشراف

د. حمزة الزبدي

الملخص

المقدمة

اعتلال الشبكية السكري واحد من المضاعفات المرتبطة بمرض السكري غير المتحكم به، اعتلال الشبكية السكري هو أحد الاسباب الرئيسية التي يمكن الوقاية منها لضعف البصر في العالم كما أنه السبب الرئيسي للعمى لدى البالغين دون سن 75 عاماً في البلدان النامية. في هذه الدراسة هدفنا الى معرفة نسبة انتشار اعتلال الشبكية السكري والعوامل المرتبطة به بين مرضى السكري في الضفة الغربية.

اسلوب وطريقة البحث

أجريت دراسة مقطعية كمية في كل محافظات الضفة، خضع كل المرضى الى فحص عيون شامل اضافة الى عينات دم وبول، استخدمت استبانة الكشف المبكر لاعتلال الشبكية السكري لجمع المعلومات والبيانات من المرضى.

النتائج

كانت نسبة انتشار مرض اعتلال الشبكية السكري (DR) في الضفة الغربية هي 41.8٪. كانت نسبة المرضى باعتلال الشبكية (NPDR) هي 50.3٪ (اعتلال الشبكية (NPDR) المعتدل كانت 38.5٪، اعتلال الشبكية (NPDR) المعتدل 10.6٪، اما اعتلال الشبكية (NPDR) الحاد كانت نسبته 1.2٪). بينما كانت نسبة اعتلال الشبكية السكري (PDR) 9.9٪ وأما اعتلال البقعة

الصفراء السكري (DME) كانت نسبته 6.8٪. ارتبط اعتلال الشبكية السكري بشكل كبير بالعوامل التالية (مؤشر كتلة الجسم، المدة الزمنية لمرض السكري، نسبة البروتين الدهني منخفض الكثافة، ونسبة البروتينات في البول).

الخلاصة

الكشف المبكر عن مرض السكري واعتلال الشبكية السكري من شأنه ان يساعد على السيطرة والوقاية من اعتلال الشبكية السكري. كما يمكن للبرامج التوعوية المتركزة على السكان والتقييم الطبي المستمر ان تساعد على تحسين الحالة الصحية والادارة الذاتية والحد من المضاعفات والمرتبطة بهذا المرض.