Deanship of Graduate Studies

AL-Quds University

Determinants of Diabetic Eye Complications Among St. John Eye Hospital Community Clinics Attendants

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M.Sc. Thesis

Jerusalem-Palestine

1430/ 2009

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A thesis submitted in partial fulfillment of requirements for the degree of master of public health program to the Faculty of Public Health/ Al-Quds University

1430/ 2009

Al-Quds University

Deanship of Graduate Studies

Applied School of Public Health

Thesis Approval

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Master thesis submitted and accepted, Date: 15/09/2009 .

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Jerusalem – Palestine

1430 / 2009

Dedication

To my dear parents whom I own them all means of dignity and gratitude.

To my wife Maha and my kids Ahmad and Malak.

To all teachers who ever taught me.

Nasrallah Awad Oudatalla Khalilia

Declaration

I certify that this thesis submitted for the degree of Master is the result of my own research, except where otherwise acknowledged, and that this thesis (or any part of the same) has not been submitted for a higher degree to any other university or institution.

Signed:

Nasrallah Awad Oudatalla Khalilia

Date: September 15th 2009

Acknowledgment

I would like to extend my deepest gratitude to my advisor Dr. Lina Al-Khairy who gave me all means of support to accomplish my thesis.

A lot of thanks go to the staff of Faculty of Public Health for the valuable courses they taught me in the Masters program.

Special thanks go to my matron Mrs. Jacky Juidy and St. John Eye Hospital staff for their big support and friendly assistance, I greatly appreciate their help.

I owe my thanks more than I can express to my parents, wife, brothers, sisters and my lovely kids Ahmad and Malak for their inspiring, caring and endless support throughout my study.

Finally, all gratitude to my friends wherever they are for their various support and care.

Abstract

Diabetes mellitus is of high prevalence in the Palestinian community, reaching up to 9% (State of Palestine- Ministry of Health, August, 2005). Diabetic eye complications have a significant impact on visual status. Better control of diabetic eye determinants like duration of diabetes, hypertension and blood glucose level greatly hinders progression and the effect of diabetic eye complications. Neither prevalence nor the determinants of diabetic eye complications have ever been studied in the Palestinian community.

The study objectives are to estimate the prevalence of the main diabetic eye complications and visual impairment among a sample of Palestinian diabetics**.** Additionally, to investigate the association of selected diabetic eye risk factors on the development of the main diabetic eye complications and visual status.

The current study is a cross-sectional study. A random sample of three months period (1st January 2007 – 31 March 2007) was selected to represent the whole year of 2007. During the study time frame, the medical files of 420 type 1 and type 2 diabetic patients who were screened by Saint John Hebron Center (99 patients) and Saint John Outreach clinic (321 patients) were included in the study. We estimated the prevalence of diabetic eye complications (diabetic retinopathy, cataract, glaucoma) as well as their association with selective diabetic risk factors; namely, gender, type of diabetes, hypertension, duration of diabetes, age and clinical settings. The Statistical Package for Social Sciences-software version 13 (SPSS) was used for analysis. Univariate analysis of all independent variables with the two outcome variables, i.e. diabetic eye complications and visual impairment was done. Binary logistic regression analysis was used for multivariate analysis; all independent variables were included in the model to test their effect on both diabetic eye complications and visual impairment

Among the study participants, results showed that 41.7% were males and 58.3% were females. The mean (SD) of age was 58.6 (9.30) years, diabetes duration 11.5 (7.48) years and HbA1c 8.3 (1.7). Out of the total, only 22.6% of subjects had normal HbA1c value ≤7. A 32% of the study participants with diabetes duration 0-5 years were found having diabetic retinopathy. Retinopathy, cataract and glaucoma were present in 66.6%, 25.5% and 9.5% of the study participants, respectively. Out of the total study participants, visual impairment was present in 35.7%. Males were found to be more likely to have diabetic eye diseases than females, especially retinopathy. Diabetic retinopathy, cataract and glaucoma contributed to (31%), (6%) and (0.7%) of visual impairment respectively. Univariate analysis showed that subjects who were at increased odds of developing diabetic retinopathy were males, hypertensive patients, having longer diabetes durations and patients between 60-65 years old. However, after adjusted to all independent variables in the study, only male gender, duration of diabetes and age group category 60-65 years remained statistically significant independent risk factors for retinopathy. At the Univariate analysis,

hypertension, age and duration of diabetes ≥16 years were found significantly associated with cataract formation.

However, adjusted logistic regression analysis revealed that only patients who were ≥ 60 years old were at increased odds of developing cataract. Among the determinants, only HbA1c level ≥ 9.2 was found to be statistically significant associated with glaucoma development even after adjustment to all risk factors that were investigated in the study. Our results showed that subjects who were statistically significant at increased odds (crude and adjusted) of having visual impairment were hypertensive patients, who were ≥ 60 years old and having diabetes for ≥ 11 years.

We conclude that both, diabetic eye complications and visual impairment were highly prevalent among the study participants especially among men. Diabetic eye determinants were found to be associated with diabetic eye complications as found in the literature. Retinopathy was found to develop earlier and hypertension seemed to be underestimated among our study participants compared with what was described in the literature. Better management of the modifiable risk factors like early detection and proper glycemic control is beneficial in minimizing diabetic eye complications. More studies are needed to explore the effects of other potentially important determinants of diabetic eye complications in the Palestinian community.

الملخص:

يعتبر مرض السكري من أكثر الأمراض المنتشره في فلسطين، وتعتبرمضاعفاته على العين البشريه ذات أثار سلبية على ضعف الرؤيا. لهذا فان ضبط عوامل الخطرالمرتبطة بمرض السكري مثل العمر، الفترة الزمنية للإصابة بمرض السكري، ضغط الدم ومعدل مستوى السكر التراكمي في الدم ذات أثر ايجابي في تفادي أو الحد من مضاعفات السكري على العين البشرية. يذكر أن نسبة انتشار مضاعفات مرض السكري المتعلقة بالعين، وكذلك عوامل الخطر المرتبطة بها لم يتم دراستها من قبل في المجتمع الفلسطيني.

تهدف هذه الدراسة إلى وصف نسبة انتشار مضاعفات مرض السكري المرتبطة بالعين بما في ذلك ضعف الرؤيا الناتجة عن هذه المضاعفات بين عينة من مرضى السكري في فلسطين. كذلك ان الدراسة تهدف إلى وصف وتقدير مدى ارتباط عوامل الخطر لمرض السكري بمدى إنتشار وتطور مضاعفات مرض السكري على العين البشرية وما يترتب عنها من ضعف الرؤيا.

اتبعت هذه الدراسة المنهج الوصفي المقطعي. كانت عينة الدراسة عشوائية حيث تم اختيار الثلاثة شهور الأولى من سنة 2007 عشوائيا بما يناسب الإطار الزمني المحدد والضيق للدراسة و لجمع المعلومات اللازمة لها. لقد شملت الدراسة جميع الملفات الطبية الخاصة بمرضى السكري من النوع الأول والثاني (420 مريض) والذين تم فحصهم في عيادات مشفى سانت جون للعيون (عيادة العيون المتنقلة 321 مريض، وعيادة سانت جون للعيون \ الخليل 99 مريض) في الفترة الزمنية ما بين الأول من كانون الثاني حتى الحادي والثلاثين من آذار من سنة 2007.

كانت نسبة الذكور في عينة الدراسة 41.7% من المشاركين فيها ونسبة الاناث 58.3%. وكان متوسط أعمار المرضى 58.6 سنة (الانحراف المعياري = 9.3)، أما متوسط المدة الزمنية للإصابة بمرض السكر فكانت 11.5 سنة (الانحراف المعياري = 7.48). أما متوسط نسبة تركيز السكر التراكمي في الدم فكانت 8.3 (الانحراف المعياري = 1.7 . وكذلك تبين أن نسبة قليلة من المشاركين في الدراسة (22.6%) كانت نتائج فحص HbA1c ضمن المعدل الطبيعي (HbA1c ≤7)، بينما أظهرت النتائج أن (32.0%) من المرضى كانوا مصابون باعتلال شبكية العين علما أن المدة الزمنية لإصابتهم بمرض السكري كانت بين (0- 5) سنوات. وأظهرت نتائج الدراسة أن نسبة انتشار مضاعفات السكري لكل من مرض اعتلال شبكية العين، عتامة عدسة العين (الكاتاراكت أو المياه البيضاء) وارتفاع ضغط العين (الجلوكوما أو المياه السوداء) كانت 66.6%، 25.5% و9.5% على التوالي. لقد وجد أن 35.7% من بين المشاركين في الدرسة مصابون بضعف الرؤية. كذالك وجد أن الرجال كانوا أكثر عرضة لأمراض العيون الناتجة عن مرض السكري من النساء. وأظهرت الدراسة أن كل من اعتلال شبكية العين، المياه الزرقاء والجلوكوما كانت قد ساهمت في (31.1%)، (6.0%) و(0.7%) في ضعف الرؤيا على التوالي.

وأظهرت نتائج الانحدار اللوجستي (الغير معدل) أن كل من عوامل الخطر، الرجال، ضغط الدم، الفترة الزمنية للإصابة بمرض السكري والعمرمن 60-65 سنة كانت ذو ارتباط ايجابي ومساهم

بشكل إحصائي في تطوراعتلال شبكية العين. ولكن نتائج الانحدار اللوجستي (المعدل) بينت أن الرجال، الفترة الزمنية للإصابة بمرض السكري والعمر من 60-65 سنة هي وحدها التي حافظت على ارتباطها الإيجابي وبشكل إحصائي مع تطوراعتلال شبكية العين. وكانت نتائج الانحدار اللوجستي (الغير معدل) قد اظهرت أن كل من عوامل الخطر، العمر ضغط الدم و الفترة الزمنية للإصابة بمرض السكري $\geq$ 16 سنة هي وحدها التي ترتبط بشكل إحصائي مع تطور المياه الزرقاء. في حين أن نتائج الانحدار اللوجستي (المعدل) بينت أن العمر$\leq$ 60 سنة هو عامل الخطر الوحيد الذي يرتبط بشكل إحصائي مع تطور المياه الزرقاء. لقد أوضحت نتائج الانحدار اللوجستي (الغير معدل والمعدل) أن نسبة تركيز السكر التراكمي في الدم (HbA1c =9.2) هي وحدها المحددة والمرتبطة بشكل إحصائي بتطور الجلوكوما. بينما أظهرت نتائج الانحدار اللوجستي (الغير معدل و المعدل) أن كل من عوامل الخطر، ضغط الدم، العمر$\leq$ 60 سنة و الفترة الزمنية للإصابة بمرض السكري $\geq$ 11 سنة كانت ذو ارتباط إيجابي ومساهم بشكل إحصائي مع تطور ضعف الرؤيا.

لقد بينت الدراسة أن الرجال كانوا أكثر عرضة من النساء للإصابة بمضاعفات مرض السكري على العين وضعف الرؤيا. وكذلك تبين أن تطور اعتلال شبكية العين لدى المشاركين في هذه الدراسه كان قد تطور بشكل مبكر مقارنه مع مجتمعات أخرى، في حين أن نسبة تشخيص والكشف الإكلينيكي لضغط الدم كانت دون المعدل العام مقارنه مع مجتمعات أخرى. أن ضبط عوامل الخطر القابله للتعديل مثل الفحص والتدخل الطبي المبكر، ضبط تركيزالسكرفي الدم ذات فعاليه كبيره في تحجيم و تقليل مضاعفات مرض السكري على العينين. ومن هنا لابد بالقيام بدراسات أوسع وأعمق في هذا المجال ليتسنى التعرف بشكل أفضل على محددات أخرى لمرض السكري على العين في المجتمع الفلسطيني.

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Conceptual definitions,

The following conceptual definitions were adopted from (Kanski J, 2003) and (Johnson et al, 1998).

Age related macular degeneration (AMD): Is a disease associated with aging that gradually destroys sharp, central vision.

Applanation Tonometry: A slit lamp attached device for intraocular pressure measurement.

Anterior chamber: Space between the cornea and the crystalline lens , which contains aqueous humour.

Anterior ocular segment: Part of the eye anterior to the crystalline lens, including the cornea , anterior chamber, iris and ciliary body.

Aqueous humour: Transparent fluid occupying the anterior chamber and maintains eye pressure.

Best corrected visual acuity (BCVA): Best possible vision a person can achieve with corrective devices, measured in terms of Snellen lines on an eye chart .

Cataract: Opacity of the eye lens leading to visual impairment, treated with cataract surgery (removal of the eye lens and replaced with an artificial one).

Closed angle glaucoma: Glaucoma conditions occurring suddenly due to the closed drainage angle.

Conjunctiva: Translucent protective membrane which covers the sclera.

Corneal opacity: opaque cornea- loss of corneal transparency.

Detached retina: A retinal detachment occurs when the retina is pulled away from its normal position (separation of the neural retinal from the pigmented structure).

Diabetes type 1: Insulin dependent, resulting from destruction of the insulin producing pancreatic islet cells, usually appears early in life (before 30 years old).

Diabetes type 2: Non-insulin dependent, resulting from tissue resistance to insulin or defect in the body system of utilizing the hypoglycemic insulin, usually appears late in life-after 30 years of life. Treatment could include diabetic tablets, insulin, both and diet.

Diabetic retinopathy: Pathological changes in the retinal blood supply due to raised blood glucose levels; haemorrhages, low tissue perfusion and ischemia ending up with neuroretinal damage and visual dysfunction.

Diopter: Unit of measure of the refractive power of an optical lens (equal to the power of a lens with a focal distance of one meter).

Funduscopy: Examination of the posterior segment of the human eye so as to assess the retinal, optic nerve and adjacent tissue.

Glaucoma: An eye disease characterized by abnormally increased intra-ocular pressure which leads to neural eye damage and visual loss.

Slit lamp: A microscopic device used to examine ocular tissues.

Intraocular pressure (IOP): Fluid pressure within the eye created by the continual production and drainage of aqueous fluid in the anterior chamber .

Macula: The part of the retina that is responsible for the acuteness of vision.

Macular oedema: Collection of fluid in and under the macular portion of the retina .

Magnification lens: Hand held magnification optical lens of 90 or 78 Diopter (power) used for visualization of the retina

Neovascularization: Involves the formation of new blood vessels due to ischemia of the original tissue, the new vessels are often fragile which rise for bleeding.

Open angle glaucoma: Glaucoma conditions of long duration (chronic), where the drainage angle is opened.

Optic disc: The head of the optic nerve that is formed by the meeting of all retinal nerve fibers.

Pin hole: An eye cover with holes in the middle so as patient can look through; it corrects the refractive error and estimates the best corrected visual acuity if there are no eye glasses.

Posterior lens capsule opacity (PCO): post cataract surgery (lens extraction), the remaining posterior lens capsule gets opaque which leads to reduced vision temporarily until opened with laser shots.

Pterygium: Growth of the eye conjunctiva towards the eye cornea.

Pupil: Black circular opening in the center of iris through which light passes into the crystalline lens. It changes size in response to how much light is being received by the eye.

Retina: The inner most layer of the eye coat responsible for picking up light impulses and transmit them to the brain where seeing takes place.

Retinal diseases: retinal and macular pathological findings other than retinopathy, detachment and vascular occlusions.

Sclera: the white protective opaque fibrous eye layer which coats the eye.

Snellen chart: A diagnostic chart board with a black C shape letters of different sizes used to measure visual acuity.

Squint: imbalance and lack of coordinated eye movements.

Tonometry: procedure for the measurement of intraocular pressure. A test for glaucoma.

Uncorrected visual acuity (UCVA): Best possible vision a person can achieve without corrective lenses or pin hole measured in terms of Snellen lines on an eye chart .

Vascular occlusion: retinal artery or vein obstruction (occlusion).

Visual acuity: The acuteness of vision measured by a Snellen chart.

Uveal tract: the pigmented middle eye layer which is composed of the iris, ciliary body (pigmented structure responsible for production of Aqueous humor) and Choroid (the vascular layer of the eye lying between the retina and sclera).

Uveitis: inflammation of the uveal tract layer.

Comorbidity: eye diseases that were documented in the study participants medical records (other than the main diabetic eye diseases-retinopathy, cataract, glaucoma) including:

- Retinal detachment and/or vascular occlusions: retinal detachment or / and retinal artery or vein obstruction (occlusion) that were documented in the patients medical records.

- Corneal opacity: opaque cornea- loss of corneal transparency.

- Combined causes: having more than one co-morbidity.

- Others: include the following co-morbidities: uveitis, PCO, squint, old eye surgical complications, pterygium and retinal diseases.

Acronyms

DM: diabetes mellitus

DR: Diabetic retinopathy

MoH: Palestinian ministry of health.

n : Number

PCO: posterior lens capsule opacity

POAG: Open angle glaucoma.

PP: Pages

PSC: Posterior sub-capsule eye lens cataract

SD: Standard deviation

UK: United Kingdom

UNRWA: United Nations

USA: United States of America

VI: visual impairment

WHO-VI: visual impairment according to WHO definition

Vol. : Volume

Vs. : versus

WHO: World Health Organization

Chapter One. Introduction

1.1 Background

1.2 Problem Statement

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1.1 Background

Diabetes is a chronic disease of lifelong duration. It threatens the quality of life of patients, persons' productivity and health care system expenditure due to its acute and chronic complications. Diabetes is a significant cause of disability and death in many countries (Shazly et al, 2000). Diabetes mellitus is prevalent in the Palestine territories. This necessitates careful measurement in terms of its complications. According to the World Health Organization, prevalence of diabetes is expected to increase in Palestine; the figures should be revised to better estimate the distribution of the disease. This will enable health care providers to better adopt more effective health care strategies. It had been estimated that the prevalence of diabetes mellitus in Palestine about 9% in 2000. It is around the reported prevalence in Egypt and Tunisia (9%) and less than in Saudi Arabia 12% and Oman 13% (State of Palestine-Ministry of Health, August, 2005).

Diabetes mellitus is one of the widely distributed diseases that exerts devastating destructive effects upon the vascular system. Microvascular changes as a result of diabetes eventually result in retinopathy, angiopathy and nephropathy. However, macrovascular changes lead to cardiovascular complications. These complications are mostly exacerbated by chronically raised blood glucose levels. One of the most common complications of diabetes mellitus is visual impairment caused by diabetic eye complications (Mason and Melville, 2000).

Diabetic retinopathy is the most well known ocular complication of diabetes. It is a leading cause of blindness among the working age group. A range of ocular diseases is also associated with diabetes. Cataract and glaucoma are serious sight threatening ocular diseases associated with diabetes. In major clinical trials, tight control of blood glucose level and hypertension has been demonstrated to reduce the risk of visual impairment among diabetic patients. Age, duration of diabetes, hypertension, obesity and blood glucose level, are all ocular diabetic risk factors of high magnitude. The public health value of intervention programs that aim at controlling such risk factors are of great importance in preventing diabetic eye diseases and visual impairment (Mancia, 2007). Proper management of diabetic eye complications remains an important public health strategy in avoiding visual impairment (Jeganathan et al, 2008).

Although the majority of blinding eye diseases is preventable or curable, blinding eye diseases remain a major socioeconomic problem in the developing countries (Tabbara, 2001).

On this basis, the investigator intends to estimate the frequency of diabetic eye complications and related visual impairment among a sample of diabetic patients that have been screened by St. John Eye hospital. Additionally, he will explore the

level of diabetic management among the study participants through investigating the effect of selected diabetic eye risk factors on the development of diabetic eye complications and visual status.

1.2 Problem Statement

The socio-economic development in the Eastern Mediterranean countries has led to an acute rise in the incidence of diabetes mellitus (Tabbara, 2001). Several risk factors like duration of diabetes, hypertension, age and glycaemic control have been identified by both cross-sectional and prospective studies as risk factors for the development of diabetic eye complications. Aggressive management of diabetic risk factors could reduce the number of visually impaired diabetic patients, especially from retinopathy (Tapp, 2003). Clinical management of diabetes maintains diabetic control and further prevents the long term complications of retinopathy, cataract, glaucoma and other associated ocular diseases (Johnson et al, 1998).

Cataract, diabetic retinopathy and glaucoma are leading causes of visual impairment amongst Palestinians. In Palestine, the incidence of blindness is around 17 per 1000 people among the general population, it is estimated that 80% of this blindness is preventable (St. John Eye Hospital, January 2004). In Palestine, there have been no studies that estimated the impact of diabetes mellitus on visual status among diabetic patients. In addition, there has been few data on visual impairment or blindness which has compromised effective health care planning and interventions concurrent with available resources (Maali, 2003).

It is a fundamental step to estimate the magnitude of diabetic eye complications, its determinants and related visual impairment among diabetic Palestinians. This allows better planning for cost effective health care interventions to minimise the burden of visual impairment and related disability consequences.

1.3 Justification of the Study

As mentioned earlier in this chapter, diabetes mellitus is a prevalent disease in Palestine. It is expected that the incidence of diabetes mellitus will increase among Palestinians in the coming few years because diabetic risk factors are increasing. Abdul-Rahim et al reported that diabetes mellitus risk factors and other heath conditions which exacerbate diabetes and its complications are of high magnitude among Palestinians. Obesity and central obesity are prevalent in the urban Palestinian population. Their associations with diabetes, hypertension, and dyslipidaemia point to a potential rise in diabetic complications and cardiovascular diseases (Abdul-Rahim et al, 2001). Ocular manifestations like glaucoma, cataract and macular degeneration were found associated with obesity in many epidemiological investigations (Bohlman, 2005). In Palestine as in other Middle East countries, un-operated cataract remains the leading cause of visual impairment and blindness. Whereas, diabetic retinopathy has recently been recognised as the second most common cause of visual impairment and blindness (Maali, 2003). In

Palestine, there is fragmentation in reporting and managing system regarding diabetes mellitus. This lack of information leads to inability to estimate the cost and resources required for appropriate decision-making regarding diabetic management (State of Palestine- Ministry of Health, August 2005).

Because the study is restricted to a time frame and within limited resources, it was difficult to conduct a representative study on the national level that would better shed the light on the features of diabetic eye complications among Palestinians. However, the current study has used a sample of diabetic patients' data that was collected by the main provider of eye care services in Palestine, namely St. John eye hospital settings in West Bank. St. John outreach mobile eye clinic represents a host for a diversity of Palestinian diabetic patients throughout West Bank. On the other hand, St. John Eye Hebron center is also the largest and the main provider of different diabetic eye care services to the largest Palestinian governorate. The study findings will reflect the prominent features of diabetic eye complications on a wide spectrum of Palestinian diabetics since the geographical background of the study patients is the whole West Bank territory. Upon the study findings, the ultimate assumption is that the interested health care settings would consider the study results in their future planning and implementing diabetic eye care programs. Ethically, the research various phases are neither experimental nor invasive in nature, where by either way it would not harm the study participants neither physically nor psychologically.

The above discussion reveals the wide range distribution of diabetes mellitus and its associated risk factors (impaired glucose tolerance, hypertension, obesity) among Palestinians. All are predisposing factors for the development of ocular eye diseases among diabetics in Palestine. Estimating the magnitude effect of diabetic eye risk factors on the development of ocular complications and related visual impairment will further support the efforts of combating diabetic eye complications among Palestinians. On this basis, the researcher planned to carry out this baseline study to be the first research paper that has ever investigated diabetic eye complications in the Palestinian community.

1.4 Overall aim of the study and its objectives

The overall aim of the study is to investigate the effect of diabetic eye risk factors (duration of diabetes, age, hypertension, type of diabetes, blood glucose level) on the development of the main diabetic eye complications (retinopathy, cataract, glaucoma) and related visual impairment among the study participants.

1.4.1 Objectives:

The study sets out to achieve the following objectives:

1. Identify the prevalence of the main diabetic eye complications among the study participants namely diabetic retinopathy, cataract and glaucoma.

2. Determine the prevalence of visual impairment among the study participants.

3. Examine the association between diabetic eye risk factors (duration of diabetes, age, sex, hypertension, type of diabetes and blood glucose level) and the development of diabetic eye complications and visual impairment.

1.5 Feasibility of the study and assumptions

The study has received all means of encouragement and support from both the hospital research ethical committee and medical staff. The research ethical requirements have been approved and the related approval form has been signed by the hospital research ethical committee. It was further handed over to the university/ Faculty of Public Health. The following points had facilitated the accomplishment of the thesis:

- The investigator himself is the in charge of community health department and the outreach mobile eye clinic at St. John Eye Hospital. He completed post graduate studies in ophthalmic field with seven years experience in ophthalmic nursing and clinical eye examination. Such qualifications had been very supportive for the investigator to be fully aware and oriented with the topic being studied which in turn facilitates the accomplishment of the study.

- The cooperation and contribution of the hospital professional staff have facilitated the completion of this study through their positive role in the data collection phase of this study. Their ophthalmologic theoretical and clinical background have assisted in having a valid collected data.

- The availability of database (patients' medical records) has provided the needed data to complete the study in a sensible time and cost to cover the overall study objectives.

- The library of St. John Eye hospital is rich in ophthalmic periodic journals and text books which underpin the study accomplishment.

1.6 Limitations of the study

A- Regardless of the fact that St. John Eye Hospital care settings is one of the main eye care providers in West Bank territories, some patients wouldn't have the opportunity to be part of the study (selection bias) due to the followings:

1. Some patients, due to their deteriorating visual status, lack of companionship support could not attend St. John Eye Hospital care settings for check up.

2. Due to the current limited accessibility to the Palestinian communities and health care settings; there should be some sort of excluding diabetic patients as they could not make it and reach St. John Eye Hospital care settings for check up.

3. The study sample was taken from an ophthalmic eye care setting attendants. It is expected that the prevalence of diabetic eye diseases and related visual impairment would be higher than it is in the general population. Hence the study results could not be generalized to the whole number of diabetics in West Bank. Rather, it reflects the status of diabetic patients that were screened by St. John eye Hebron clinic and Outreach program in the year 2007.

B-Limitations as a Cross-sectional study:

1. Documentation problems: the individual medical records did not show some of the needed information. Smoking habits, level of education, obesity, life style and diet as determinants of diabetic eye complications were not documented well in the medical records.

2. A cross sectional design precludes definitive causal associations. Thus, interpretation of the current study results should be made with caution.

1.7 Overview of the paper progression and chapters

A consistent detailed explanation of the study different phases and progression has been explored in the chapters; introduction, literature review, conceptual framework, methodology, results and finally discussion, conclusion and recommendations. In chapter one, I have presented the most relevant background information regarding diabetic eye complications, its risk factors and related visual impairment consequences. Additionally, the chapter introduced the magnitude effect of diabetes upon ocular structure and function. Problem statement, justification of conducting the study and its objectives were also discussed. It further identified the feasibility and limitations aspects. Chapter two highlighted the relevant literature regarding diabetic eye diseases, risk factors and related visual impairment consequences. It also explored some related national visual impairment figures. The study conceptual framework has been stated and explained in chapter three where the reader can build an insight about the theoretical platform of the study main concepts. Chapter four of the thesis included the study methodological approaches including, design, sampling, objectives, variables, limitations and analysis methods. The last two chapters dealt with the study core investigation and overall aim where data results and discussion have been presented respectively. Finally, the thesis ends up with recommendations concerning the overall subject and related implications.

Chapter Two. Literature review

2.1 Introduction

2.2 Visual impairment and diabetes

2.3 Visual Impairment in Palestine

2.4 Association between diabetes and ocular diseases

2.5 Main diabetic eye risk factors

2.6 Summary

2.1 Introduction

The literature review in this chapter will firstly highlight the magnitude effect of diabetes mellitus on visual impairment. Some relevant research findings regarding visual impairment among Palestinians will be explored. Later, the chapter will discus the main diabetic eye diseases (DR, cataract and glaucoma) that were explored by the literature. Finally, a number of selected diabetic eye risk factors and their impact on diabetic eye complications will be highlighted.

2.2 Visual impairment and diabetes

Diabetic eye diseases are of high magnitude in the developing countries due to the recent increase in life expectancy and the growing incidence of diabetes (Sharma, 1996). Different estimates of diabetic eye diseases among different groups and settings were reported by different epidemiological studies. This difference is mostly due to different epidemiological approaches and variations in the characteristics of participants. However, no doubt that diabetes mellitus is one of the systemic diseases that seriously affect different eye tissues, namely the retina. Hence, it heavily precipitates visual impairment (Johnson et al, 1998).

In 1999, out of the 85447 surveyed persons in USA, 3391(4.0%) were diabetics. The overall prevalence of visual impairment was 24.8%. It was significantly associated with increased age and more common in females than males (27.4%vs 21.6%). After adjustment for age, the odds of having impaired vision were 70% higher for persons with type 1 diabetes (odds ratio (OR = 1.7) and 40% higher for those with type 2 diabetes who used insulin (OR = 1.4) compared with nonusers. Among insulin users, the age-adjusted odds did not differ by type of diabetes. The risk of visual impairment is greater for persons who use insulin than for those who do not. Hence, the effect of socio-demographic, type of diabetes treatment, and access to and use of health care services were considered important determinants of visual impairment among diabetics (Saaddine et al, 1999). Prevalence of blindness among a sample of Jordanian diabetics (a survey of 986 Diabetic participants) was found to be 7.4%, where as 10.1% were visually impaired. Sex, age and duration of diabetes were found significantly associated with visual impairment (Till et al, 2005). In Sweden, a case-control study by Olafsdottir et al found that prevalence of visual impairment and blindness among the diabetic group was (10.2%) and (2.9%) respectively. Factors like increasing age, diabetes duration and blood pressure control were found to be significantly related to worsening of best corrected visual acuity among the diabetic patients. For HBA1c, the level of glycemic control did not show statistical association with visual status among the diabetic group (Olafsdottir et al, 2007). Type 2 diabetes and hypertension are frequently associated. In fact hypertension among diabetics exacerbates visual impairment. Matthews D et al found that the absolute risks of blindness in one eye for the tight blood pressure control group (3.1 per 1000 patient/years) was much lower compared with less tight blood pressure control group (4.1 per 1000 patient/years).

Hypertension is a risk factor for visual impairment due to the destructive effects upon the retina. Stress of the high blood pressure induces damage to vessel walls which eventually precipitates worsening of vision (Matthews et al, 2004).

2.3 Visual Impairment in Palestine

To our best knowledge, there are no studies that estimated the prevalence and causes of visual impairment among diabetics in Palestine. However, few studies examined the prevalence of visual impairment among Palestinians. In 1984, a study (9548 subjects from West Bank and Gaza Strip, 55.4% females and 44.6% males) has shown that the prevalence of low vision in Palestine was 6.8%. Prevalence of binocular blindness was 1.7%. Cataract, trachoma and corneal opacity were found to be the leading causes of blindness. There were significantly more blind females (65.5%) than males (34.5%). Blindness increased with age; 40% over 80 years and nearly 50% over 90 years were blind. The percentage of blindness in the economically active age group of 20-60 years was 1.4% (Chumbley and Thompson, 1984). Golychev V in his study (1427 subject from west Bank and Gaza Strip) concluded that Palestine suffers a high incidence of ophthalmic diseases. Conjunctivitis, cataract, corneal opacities, retinal dystrophies, congenital conditions and diabetic retinopathy were found prevalent in Palestine. Blindness resulted mainly from corneal opacities and congenital eye diseases. Relative marriages appear to play an essential role (Golychev, 1991). Among the disabled persons in the South of West Bank, it was found that 9.1% had sight disability (15.1% had mental disability, 35.3% had physical disability and 14.2% had hearing disability), (State of Palestine, Palestinian Central Bureau of Statistics, October 1998). The demographic and health survey in West Bank and Gaza Strip for the year 2004, showed that 1.7% of the surveyed subjects had disability of some type. The highest percentage was for the "movement disability" (29.8) followed by "seeing disability" (18.7). In West Bank, seeing disability was the second category (20.9) among all types of disabilities. In Gaza, The highest percentage of disability was 33.0 for movement disability, where seeing disability had fallen in the 3rd category (14.4). In West Bank, 43.8% of the total seeing disability was due to general health diseases while congenital causes accounted for 17.7% (State of Palestine, Palestinian Central Bureau of Statistics, June 2005). A Palestinian study based upon a mobile eye clinic data found that 64% of the participants had either visual impairment or blindness at least in one eye. Of those, (7.7%) have had bilateral visual impairment and (3.4%) have had bilateral blindness. Un-operated cataract was the most common cause of visual impairment. 17.5% had either blindness or visual impairment as a result of diabetic retinopathy. Glaucoma accounted for (8.8%) of visual impairment or blindness (Maali, 2003). The latest Palestinian survey which investigated disabilities in Tulkarem and Qalqilia districts (50,053 persons) revealed that 10.9% of the study participants have ophthalmic disability. 11.4% of the total ophthalmic disabled were 18 years and over. Females (12.0%) were more affected than males (10.3%). Economic hardship and psychological complains were the main problems that face the ophthalmic disabled persons. The survey has highlighted the shortage of ophthalmic care and rehabilitation programs in Palestine. It recommended the

need of Mobile eye care programs as a sharp tool to make eye care services accessible (Akhrass and Hamdan, 2006).

2.4 Association between diabetes and ocular diseases

Diabetic patients are more prone to ocular diseases and visual impairment more than patients free of the disease. Diabetes exerts structural and functional eye changes due to the destructive effects of pathological microvascular and ocular tissue alterations. A range of pathological findings including retinopathy, cataract, glaucoma and corneal opacity were found to be associated with diabetes mellitus (Johnson et al, 1998), (Sharma, 1996). While retinopathy remains a leading cause of visual impairment, other blinding diabetic eye diseases are of high magnitude among diabetic patients. People older than 65 years with diabetes have twice the risk of developing cataracts and three times the risk of developing glaucoma than those without diabetes (Mohamed et al, 2007). In Addition, retinal detachments and retinal vascular occlusions are more likely to develop in diabetics than non-diabetics (Kanski, 2003). The findings of the National Health Survey-2002 for persons aged $\geq$50 years (NHIS-USA) showed a higher prevalence of visual impairment and eye diseases among diabetics compared with non-diabetics. Although retinopathy is a major cause of visual impairment among diabetics, other causes like cataracts and glaucoma are frequently responsible for visual impairment in such patients. The survey showed that among persons with and without diabetes, the age-adjusted prevalence of visual impairment was 23.5% and 12.4%, respectively (Saaddine et al, 2004). Similarly, Johnson G et al, reported that cataract is more common among diabetics than non-diabetics. Cataracts were found more responsible for decreased visual acuity than diabetic retinopathy in patients with type 2 diabetes as found by the WESDER study. Regarding glaucoma, at least two types of glaucoma are frequent in people with diabetes. This includes neovascular glaucoma and open angle glaucoma. Both types appear to occur earlier among diabetics and markedly associated with decreased visual acuity, (Johnson et al, 1998). Moreover, visual impairment has been estimated to be 25 times more prevalent among an Australian diabetic population compared with a non-diabetic group (Lamoureux et al, 2000).

Retinopathy is a complication of diabetes which primarily affects the retina. While its' progression is gradual, it is the most common and serious diabetic eye complication (Maskari and Elsadig, 2007), (Genuth et al, 2002). In retinopathy, macular oedema and complications from retinal neovascularization (abnormal blood vessel growth) are responsible for the majority of visual loss. When oedema involves the center of the macula, visual acuity is usually reduced, this might be temporary. With neovascularization, a permanent retinal damage including loss of the sensory cells usually result in a progressive visual loss and blindness (Murphy, 1995). In fact, during the first two decades of diabetes mellitus, nearly all type 1 diabetics and more than 60% of type 2 diabetics develop retinopathy (Fong et al, 2003). Visual impairment due to retinopathy was found to be of high magnitude in both developed and developing countries. In United States (Wisconsin Epidemiologic Study), it was found that 3.6% of type 1 diabetes and 1.6% of type 2

diabetes were legally blind. In type 1 diabetes group, 86% of blindness was attributable to diabetic retinopathy. In type 2 diabetes group, one-third of the cases of legal blindness were due to diabetic retinopathy (Fong et al, 2003). Early diagnosis and treatment of retinopathy is of optimal impact on both eye structure and function (Johnson et al, 1998). A population based study that was conducted in Australia concluded that regular screening for diabetic retinopathy and more aggressive management of risk factors could reduce the number of people who develop vision threatening retinopathy (Tapp et al, 2003).

Many epidemiological studies have investigated retinopathy prevalence among diabetic groups in different geographical settings. A prevalence rate of 50% was reported in both Mexico and UK, 31.3% in Sri Lanka and 26% was found in Pakistan (Haddad and Saad, 1998). In Turkey, Karadeniz et al, investigated the prevalence of diabetic retinopathy by evaluating the medical records of a Diabetic Outpatient Clinic. Retinopathy was diagnosed in 42.8% of patients (33.2% in type I, 45.5% in type II), (Karadeniz and Yilmaz, 2007). In Spain, prevalence of diabetic retinopathy was found to be 20.9% among the total study participants (175 patients with type 1 diabetes and 3344 patients with type 2 diabetes). In type 1 diabetes patients, prevalence of retinopathy was 25.6% compared with 14.8% in type 2 diabetes patients. In the Arab world, prevalence of diabetic retinopathy was found to be varied among different groups in different countries. It was found to be 31% in Saudi Arabia, 42% in Egypt and 8% in Kuwait (Maskari and Elsadig, 2007). To our best knowledge, no epidemiological studies have yet investigated ocular diseases and visual impairment among Palestinian diabetics. Diabetic retinopathy remains a major source of visual loss among diabetics. It is an important cause of visual loss in adults (Lamoureux et al, 2000).

Diabetes is a well-known recognized risk factor for cataract (eye lens opacities). A number of studies have established an association between diabetes and cataract (Janghorbani et al, 2000), (Kanski, 2003). Furthermore, clinical sciences have documented such association between the two diseases. Jeganathan et al, reported that cataract is a major cause of vision impairment in people with diabetes. The association between the two diseases (diabetes and cataracts) has been supported by findings from both clinical epidemiological studies and basic sciences (Jeganathan et al, 2008). Tsai et al, reported that people with diabetes tend to get cataracts at a younger age and have them progress faster (Tsai et al, 2007), (USA_American Diabetes Association, 2006). Data from the 2002 National Health Survey for persons aged $\geq$50 years (NHIS-USA) found that the age-adjusted prevalence for cataracts among those with and without diabetes was 31.8% and 21.2%, respectively. Persons with diabetes have had more cataracts than those without the disease (Saaddine et al, 2004). Harding J et al reported that while the exact mechanism for cataract formation among diabetic patients has not identified clearly, the disease remains a risk factor for cataract formation. Analysis of two case control studies in UK has shown that diabetes is a powerful and highly significant risk factor for cataract with a relative risk of 5.04 (Harding et al, 1993). Among a Brazilian diabetic group, cataract was present in 19.8%. The study concluded that the visually impaired cataract should be suspected in young diabetic patients

(Esteves et al, 2008). Diabetes was found to be a risk factor for different types of cataract such as posterior sub-capsular cataract and cortical cataract. Both cross-sectional and prospective data from three population-based studies (the Beaver Dam Eye Study, the Blue Mountains Eye Study, and the Visual Impairment Project) have found an association between diabetes and the development of both posterior sub-capsular cataract and cortical cataract. Such association was not found with nuclear cataract (Jeganathan et al, 2008). However, controversial findings regarding the association between cataract and diabetes have been documented by some studies. While some hospital-based studies have supported a positive association between cataract and diabetes, others have failed to demonstrate such association (Rowe et al, 2000). Nevertheless, cataract remains a marked cause of visual impairment among the elderly with and without diabetes (Till et al, 2005). Tsai et al, reported that previous epidemiologic studies have demonstrated that cataract is one of the most common causes of visual impairment in patients with type 2 diabetes (Tsai et al, 2007). In France, the prevalence and causes of visual impairment have been estimated in a sample of 423 Type 2 diabetic outpatients (aged 35 to 74 years). Prevalence of blindness and visual impairment was 1.2% and 7% respectively. The major cause of blindness was cataract, accounting for 38% of the cases of blindness. The study concluded that cataract remains the major cause of visual impairment in Type 2 diabetic patients (Delcourt et al, 1995).

Glaucoma is another diabetic eye disease which tends to seriously damage the neural structure of the eye due to the increased intra ocular pressure. Hence, visual loss is common among patients with glaucoma. Additionally, some studies have found an association between diabetes and glaucoma features like increased intra-ocular pressure and optic disc nerve changes. Visual loss due to glaucoma is irreversible due to optic neuropathy (MacEwen et al, 1999). Such findings were also found by several studies. Changes in the eye drainage system, increased intra ocular pressure and optic nerve alterations were all found to be common glaucoma features among diabetic patients (Till et al, 2005), (Johnson et al, 1998). In an Australian population (49-96 years old), the Blue Mountains Eye Study found that diabetic patients were at increased odds of developing glaucoma compared with non-diabetic patients. Glaucoma prevalence showed an increase in people with diabetes (5.5%) compared with those without the disease (2.8%). Ocular hypertension was also more common in people with diabetes (6.7%) compared with those without diabetes (3.5%). The authors found a significant and consistent association between diabetes and glaucoma. They further suggested that there is a real association between diabetes and open-angle glaucoma (Mitchell et al, 1997). The age-adjusted prevalence of glaucoma among those with and without diabetes in America was (8.0% versus 4.3%) respectively, as found by the National Health Survey- 2002 for persons aged $\geq$50 years (Saaddine et al, 2004). A cohort of 10 years follow up of 2366 diabetic patients showed an incidence of 3.7% of glaucoma in those patients with type 1 diabetes, 6.9% in people with type 2 diabetes not using insulin, and 11.8% in patients with type 2 diabetes using insulin (Klein et al, 1997). In fact, different forms of glaucoma were found to be associated with diabetes. Growth of pathological vessels on the eye iris and drainage angle (neovascularisation) due to diabetes, result in increased intra-ocular pressure and

end up with neovascular glaucoma. In the presence of advanced proliferative retinopathy, iris neovascularisation is exacerbated and hence neovascular glaucoma develops aggressively (Preda et al, 2006), (Allingham et al, 2005). In addition, diabetic patients were found to be significantly at increased risk of developing primary open-angle glaucoma (POAG) (Bonovas et al, 2004). In USA, it was found that the prevalence of open angle glaucoma was 40% higher in participants with type 2 diabetes than in those without the disease (USA-American Diabetes Association, 2006). Additionally, Pasquale et al, found that type 2 diabetes was positively associated with primary open angle glaucoma (RR = 1.82) even after controlling for a number of risk factors (age, race, hypertension, body mass index, physical activity, alcohol intake, smoking, and family history of glaucoma), (Pasquale et al, 2006). However, MacEwen et al reviewed all potentially relevant English language articles that investigated the association of diabetes with open angle glaucoma (POAG) from 1966 to 1997. They reported that while some studies have found an association between the two diseases, others did find such association. A case control study found that POAG was present in 4.1% in the diabetic patients compared with 1.4% in the controls. In contrast, a study that was conducted on subjects aged over 40 years, found no association between diabetes and glaucoma (odds ratio 1.03) (MacEwen et al, 1999). Similarly, Voogd S et al, found no association between diabetes and open angle glaucoma in contrast to some epidemiological investigations (Voogd et al, 2006). In conclusion, visual loss due to glaucoma is initially asymptomatic which contributes to delayed diagnosis, particularly in elderly patients, thus resulting in massive deterioration in visual status. Glaucoma remains one of the leading aggressive blinding eye diseases (Khan-Lim and Samantha, 2006), (Bonovas et al, 2004), (Johnson et al, 1998).

2.5 Main diabetic eye risk factors

Some epidemiological studies have shown that a number of factors were found to be linked with the development of diabetic eye diseases. Some of the prominent diabetic eye risk factors include age, duration of diabetes, hypertension, type 1 diabetes and metabolic control (Johnson et al, 1998). In addition, factors like smoking, sex, socio-economic status and utilization of health care system were also found to be determinants of diabetic eye diseases (Shazly et al, 2000).

Factors significantly related to the occurrence of retinopathy are age, duration of diabetes, hypertension and uncontrolled blood glucose levels (Haddad and Saad, 1998). Such risk factors were found to be related to retinopathy by different epidemiological studies. In Kuwait, prevalence of retinopathy was 23.5%. Insulin treatment, duration of diabetes, age at examination, HbA1c and systolic blood pressure were all found to be risk factors for retinopathy progression (Kharji et al, 2006). Both the two randomized clinical trials, Diabetic Control and Complication Trial (DCCT-type 1 diabetes) and UK Prospective Diabetic Study (UKPDS-type 2 diabetes) showed that glycemic control is a strong preventive measurement against retinopathy. The UKPDS found that tight blood pressure control is also associated with reduction in diabetic retinopathy (Aiello et al, 2004). Further support to the importance of controlling blood glucose and hypertension was found by different

studies (Genuth et al, 2002), (Hayany et al, 2003). In Denmark, Bek et al investigated the risk factors for diabetic retinopathy; their results showed that duration of diabetes, a high HbA1c level and high systolic blood pressure were significantly associated with the severity of the disease. However, no significant association was found between retinopathy and sex, age and diastolic blood pressure (Bek et al, 2004). Similarly, in USA, no significant differences in the prevalence of diabetic retinopathy were found with age and sex (Saaddine et al, 2004). In contrast, Maskari and Elsadig found that both age and male gender were significantly related to retinopathy among their study participants in United Arab Emirates (a house hold random sample of 513 diabetics). However, hypertension was not an independent risk factor for retinopathy (Maskari and Elsadig, 2007). Furthermore, the use of Insulin is an important factor in the occurrence and progression of retinopathy as reported by several studies. In Spain, Insulin use among type II diabetes patients showed an effect on the development of the disease. Prevalence of retinopathy was higher (48.6%) among insulin users compared with non-insulin users (4.7%). However, for all patients with retinopathy, regardless of their type of diabetes and treatment regimen, older age, longer duration of disease and insulin were found to be significant risk factors for retinopathy (López et al, 2002). In fact, different risk factors were found to be associated with retinopathy as found by several studies. High levels of urea, creatinine, triglyceride and use of insulin were found to be associated with diabetic retinopathy (Haddad and Saad, 1998), (Maskari and Elsadig, 2007). In addition, Kharji et al found that cholesterol، triglyceride and microalbumin were found to be significantly associated with the development and progression of retinopathy (Kharji et al, 2006). Moreover, Negi and Vernon reported that physical activity, utilization of health care services, body mass index and consumption of alcohol were found to have an effect on the incidence and progression of diabetic retinopathy. Although smoking causes tissue hypoxia by increasing blood carbon monoxide levels and can promote platelet aggregation, many epidemiological data show no relationship between cigarette smoking and diabetic retinopathy (Negi and Vernon, 2003). However, Tadashi T et al in Japan found that smoking was a significant risk factor for retinopathy. They concluded that patients should abstain from smoking to avoid retinopathy deterioration (Tadashi et al, 1997).

A number of studies have shown that diabetes and certain diabetic eye risk factors like duration of diabetes, age, blood glucose level and hypertension are associated with cataract development (Johnson et al, 1998). Prevalence of cataract was found to be 28% among 576 Chinese patients with type 2 diabetes. In this study, older age, longer diabetes duration and higher HBA1c were found to be significantly associated with cataract among the study participants (Lee et al, 2001). In UK, 3606 diabetic patients free of cataract were followed up from 1979-1992. Among the study participants, incidence of cataract was 10.4 per 1000 person-years. The incidence of cataract in type 1 diabetes, type 2 non-insulin-treated and type 2 insulin-treated groups were 7.1, 11.7 and 17.8 per 1000 person-years, respectively. Results showed that cataract was more common in females than males. Age was found to be a significant independent predictor of cataract for all groups. Duration of diabetes was a significant independent predictor of cataract for only type I

diabetes group. Poor metabolic control was also a significant independent predictor of cataract for type 1 diabetes group and insulin-treated type 2 diabetes groups (Janghorbani et al, 2000). However, in contrast to other studies, blood glucose measures were not found associated with cataract development in a number of studies. Rowe et al stated that blood glucose level was not found as a risk factor for cataract formation (Rowe et al, 2000). Similarly, no association was found between cataract and blood glucose levels as found by Tsai et al (Tsai et al, 2007). Age is a well known strong risk factor for diabetic cataract in several studies as reported by several studies. In USA, The National Health Survey- 2002, showed that cataract among American diabetics was found to be associated with age for persons aged ≥50 years. A prevalence of 50.3% was found among persons aged ≥65 years compared with 16.1% for persons aged 50-64 years (Saaddine et al, 2004). Similarly, Esteves F et al, found that age was related to cataract formation among a Brazilian diabetic group; patients with cataracts were older in age (Esteves et al, 2008). However, some other studies have failed to demonstrate any association between cataract prevalence and age. Harding J et al reported that the results of two case control studies found that the relative risk of cataract did not increase significantly with age within the range 50 to 79 years (Harding et al, 1993). Several studies have found that female gender is another important risk factor for cataract among diabetic patients. In fact, the relationship between female gender and cataract is believed to be due to physiological female changes with increasing age. Hormonal changes associated with older age females appear to play a role in cataract formation (Johnson et al, 1998). Grey et al reported that females were found to be associated with cataract formation among patients with type II diabetes (Grey et al, 1986). In addition, The National Health Survey- 2002, showed that cataract among Americans with type 1 and type 2 diabetics was found to be associated with female gender for persons aged ≥50 years. The survey showed that cataract was present in (37.3%) among women compared with (26.7%) among men (Saaddine et al, 2004). Similarly, Harding J et al found that females with diabetes were significantly associated with cataract formation compared with males (relative risk 7.85 versus 3.42 respectively), (Harding et al, 1993). Regarding the effect of hypertension on cataract formation, controversial findings were reported by different studies. Similar to a number of studies, Esteves F et al, found that patients with cataracts had a higher prevalence of hypertension (Esteves et al, 2008). In addition, Lee et al reported that higher systolic blood pressure was found to be significantly associated with cataract formation (Lee et al, 2001). In contrast, hypertension was not found associated with cataract development in a number of studies (Rowe et al, 2000), (Tsai et al, 2007). Furthermore, Janghorbani et al reported that neither systolic nor diastolic blood pressure had a significant independent association with cataract (Janghorbani et al, 2000). A number of studies have reported different risk factors for cataract among different diabetic groups. No association was found with cataract and both smoking and body mass index. However, patients with cataracts had a higher serum creatinine and macroalbuminuria (Janghorbani et al, 2000). (Esteves et al, 2008). Additionally, Kim S and Kim S.J reported that several epidemiological studies that were published in European countries found that advanced retinopathy and treatment with diuretics are risk factors for cataract among diabetics (Kim S and Kim S.J.,

2006). On the other hand, development of cataract among diabetic patients was found to be affected by the number of diabetic risk factors patients might have. The results by Esteves F et al, showed that there was a progressive increase in cataract frequency according to the number of risk factors, starting to rise with two or more risk factors (Esteves et al, 2008).

Glaucoma risk factors are broadly varied and numerous due to the fact that glaucoma itself is of different classifications and definitions. Moreover, glaucoma features like intra-ocular pressure, visual field defects and optic nerve features are also of different classifications. They were found to be associated with different ocular diseases. However, diabetes mellitus by itself is a risk factor for glaucoma as found by several epidemiological studies. Additionally, a range of diabetic risk factors like use of insulin, age, blood glucose level, duration of diabetes and hypertension were also found to be related to different types of glaucoma (Johnson et al, 1998). A cohort of 10 years follow up of 2366 diabetic patients revealed that age was found to be significantly associated with glaucoma in type I and type II diabetes mellitus. However, people who had longer duration of diabetes were at increased risk of developing glaucoma in type 1 diabetes and type 2 diabetes using insulin. The use of insulin was found to be significantly associated with increased risk of glaucoma in those patients with type 2 diabetes (Klein et al, 1997).The use of insulin was found to be a risk factor for increased intra-ocular pressure. Negi and Vernon reported that diabetic patients have higher intraocular pressures than the normal population. Use of insulin increases such risk (Negi and Vernon, 2003). Additionally, a certain number of diabetic determinants like uncontrolled blood glucose and hypertension were found to be risk factors for glaucoma main features including increased intra-ocular pressure and optic nerve changes (Johnson et al, 1998). Dielemans et al reported that uncontrolled blood glucose levels is a risk factor for glaucoma. It was suggested by Dielemans et al that a number of glaucoma features like increased intra ocular pressure, abnormal drainage angle and high-tension glaucoma are all associated with uncontrolled blood glucose levels (Dielemans et al, 1996). Furthermore, a direct relationship between high blood glucose levels and increased intra-ocular pressure was found by some other studies (MacEwen et al, 1999). In fact, hyperglycaemia among diabetics leads to rapid swelling of the eye lens which precipitates narrowing of the drainage angle. This eventually results in angle-closure glaucoma (Negi and Vernon, 2003). Hypertension was found to be a risk factor for glaucoma in some studies. Hennis et al reported that among persons with diabetes and hypertension, intra-ocular pressure tends to increase. Their results highlighted the increased risk of elevated intra-ocular pressure in populations with high prevalence of diabetes and hypertension (Hennis et al, 2003). However, the effect of hypertension on glaucoma is still unclear and different findings from different studies were controversial. While some studies found an association between the two diseases, others failed to find such association (Allingham et al, 2005). Chopra et al found that duration of diabetes was significantly associated with a higher prevalence of open angle glaucoma (Chopra et al, 2008). Similar findings were reported by the American Diabetes Association in which diabetes duration was shown to be positively associated with increased risk of open angle glaucoma (USA, American Diabetes Association,

2006). Nevertheless, some other studies revealed controversial findings. Pasquale et al, reported that while type II diabetes was found to be positively associated with primary open angle glaucoma, the association did not strengthen with longer duration of diabetes (RR = 2.24 for duration < 5 years versus RR = 1.54 for duration ≥ 5 years), (Pasquale et al, 2006). In fact, different glaucoma risk factors were reported by different studies. Family history, diabetes, myopia, race and hypertension were all found to be related to glaucoma (Gilany et al, 2002). In UK, Pasquale et al, followed up a cohort of women from 1980-2000. Their results revealed that female gender was found to be a significant risk factor for open angle glaucoma among diabetic women (Pasquale et al, 2006)

2.6 Summary

In this chapter, the main diabetic eye diseases were discussed. The chapter explored various diabetic eye risk factors like duration of diabetes, age, hypertension and high blood glucose levels. On the national level, we have highlighted the few studies that investigated visual impairment in the general population. The prominent findings of the reviewed literature could be summarised in the following points:

1- Diabetic retinopathy is the main diabetic eye complication. Diabetes mellitus was found to be a risk factor for both cataract and glaucoma. Visual impairment among diabetic patients is of high magnitude.

2- Longer duration of diabetes, being older in age, type 1 diabetes, uncontrolled blood glucose level and hypertension were found to be risk factors for diabetic retinopathy. The devastating effect of such diabetic eye risk factors upon the development of both cataract and glaucoma was also found in some studies. Duration of diabetes and age were the most prominent diabetic eye risk factor associated with both glaucoma and cataract.

3- To our knowledge there were no studies that investigated the magnitude of visual impairment among diabetics in Palestine.

Chapter Three. Conceptual Frame Work

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3.5 WHO definition of visual impairment

3.6 Conceptual frame work

3.1 Introduction

The conceptual framework chapter will summarise the basic concepts regarding diabetic eye diseases and their risk factors. It firstly presents a brief explanation of diabetes mellitus including its types, etiology and systemic effects. Then, the basic anatomical land marks of the human eye will be explained. Additionally, the main diabetic eye diseases namely retinopathy, cataract and glaucoma will be explored including their classifications, risk factors and related visual consequences. Finally, the chapter will highlight the WHO definition of visual impairment.

3.2 Background, diabetes mellitus

Diabetes mellitus (DM) is a multisystem disease with both biochemical and anatomical consequences. It is a chronic disease of carbohydrate, fat, and protein metabolism either because of lack of insulin or because of the presence of factors that oppose the action of insulin. The result is hyperglycaemia. Diabetes mellitus (DM) is of two types, type 1 diabetes and type 2 diabetes. In type 1 diabetes, insulin is functionally absent because of the destruction of the beta cells of the pancreas (insulin-secreting cells of the islets of Langerhans) leading to absolute insulin deficiency. The disease occurs most commonly in juveniles but can occur in adults, especially in those in their 30s. The disease can be immune mediated or idiopathic. Hence, patients need exogenous insulin to replace the human endogenous insulin so as to prevent ketosis and normalize lipid and protein metabolism. In type 2 diabetes, the basic pathological mechanism is tissue resistance to the action of insulin in the muscles or insulin deficiency. Eventually the pancreas becomes less able to produce enough insulin. The result is decreased glucose transport in muscles, elevated hepatic glucose production, and increased breakdown of fat. All of which lead to chronic hyperglycemia. Type 2 diabetes appears late in life (usually after 30 years) and treated with exogenous insulin, oral hypoglycemic agents, diet or combined treatment, (Watkins, 2003).

3.2.1 Systemic effects of diabetes mellitus:

Following is a brief description of the systemic effects of diabetes mellitus, abstracted from Watkins P, 2003 (Watkins, 2003).

Diabetes mellitus is a serious systemic disease that affects the large blood vessels (macrovascular effect) and tiny blood vessels (microvascular effect). In people with diabetes, the excess glucose eventually alters the blood vessels normal structure and function. The vessels become thicker, narrower, less elastic and sometimes blocked. This interferes with blood flow to the body organs and eventually leads to less tissue perfusion and malfunctioning. It accounts for serious structural and functional complications over the cardiovascular, nephritic, neural and ocular body organs. The main systemic effects of diabetes are:

Macro vascular effects: They are related to the heart and the larger blood vessels like the arteries (cardiovascular effects**)**. Atherosclerosis (thickening) of the artery walls, heart diseases and strokes represent the main features of diabetic macrovascular effects.

Microvascular effects: Poor circulation is primarily responsible for most of the micro vascular diseases. Micro vascular diseases are related to the small blood vessels like the capillaries that supply blood to the eyes, nervous system and the nephritic vascular network. As the circulation becomes worse, tissue perfusion becomes inefficient and then both structural and functional changes develop (neuropathy, nephropathy and ocular diseases).

- **Diabetic nephropathy:** Diabetic nephropathy typically affects the network of tiny blood vessels (the microvasculature) in the kidney glomerulus. The glomerulus is necessary for the filtration of blood. Features of diabetic nephropathy include the nephrotic syndrome with excessive filtration of protein into the urine (proteinuria), high blood pressure (hypertension), and progressively impaired kidney function. When it is severe, diabetic nephropathy leads to kidney failure, end-stage renal disease, and the need for chronic dialysis or a kidney transplant.

- **Diabetes Neuropathy:** Is a nerve disorder caused by diabetes. Over time, diabetes induces damage to the nerves around the body. There are different types of diabetic neuropathy according to the affected nerve. Peripheral neuropathy is associated with the peripheral regions of the body. These include the toes, feet, lower and upper legs, the hands and the arms. Peripheral neuropathy can easily develop into ulcers, if untreated well. In advanced stages, amputation of the whole extremity is required. Another serious type of diabetic neuropathy is Autonomic neuropathy. This type affects the organs that are supplied with the Autonomic nervous system. They include the bowels, bladder, digestive, cardiovascular and sexual organs. The disease is characterised by functional disturbances of these organs. For example, when the heart or the circulatory system is affected by autonomic neuropathy, the body's ability to adjust blood pressure and heart rate may be affected. A third type of diabetic neuropathy is called Focal neuropathy. The condition is manifested by rapid weakness of a nerve. It can cause a variety of complications like inability to focus and double vision due to the affected nerves and muscles related to the eye structure.

- **Ocular diseases:** retinopathy is the major prominent micro-vascular ocular disease associated with diabetes. It is characterised by retinal tissue damage due to diabetes mellitus. However, a range of ocular diseases like cataract, glaucoma were found to be common among diabetics. More details about diabetic ocular diseases will be illustrated in the following paragraph.

3.3 Basic anatomy of the human eye

The human eye is a complex anatomical structure. The function of the eye greatly depends on the wellbeing of its structure and relevant organs; mainly the nervous and cardiovascular systems. The main anatomical features of the human eye are illustrated in figure (3.1), (Coulter and Eric, 2000).

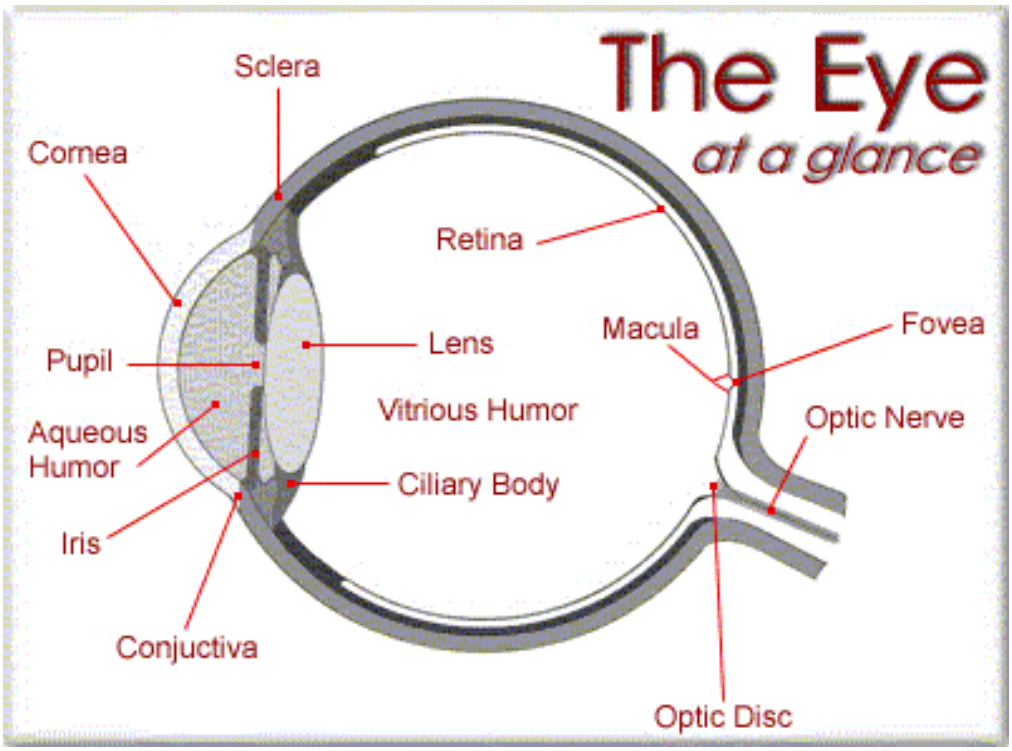

Figure (3.1): Anatomy of the human eye.

Following is a description of the main anatomical features of the human eye abstracted from (Vaughan et al, 1995),

- **The eye ball**: is the whole eye structure contained in the bony orbital cavity. It is 24.5 mm (anterior-posterior diameter).

- **Cornea**: is a dome-shaped avascular structure at the front of the eye. It is transparent, allowing light to enter the eye, and together with the lens bend and focus light onto the retina. The central thickness of the cornea is 0.5mm and 1mm at the periphery, with an axial refractive power of 43 diopters. It is composed of five distinct layers (Epithelium, Bowman's layer, Stroma, descemet's membrane, endothelium).

- **Sclera:** is the white vascular fibrous structure (collagen fibrils) which coats the eye ball. It mainly maintains the eye shape and protects the inner layers. It is 1 mm posteriorly (near the optic nerve) and 0.3 anteriorly where the Extra -ocular

muscles are attached. The sclera is covered by the conjunctiva, a thin translucent mucous membrane.

- **Iris:** It is the colored, circular part of the eye that forms the pupil in its centre (the circular opening). The iris muscles are those which control the size of the pupil; the sphincter pupillae muscle (pupil constrictor muscle) and the dilator pupillae muscle (pupil dilator muscle). The muscular structure controls the size of the pupil so as the appropriate amount of light can pass through to form an image on the retina (retinal illumination). The iris stroma contains the melanocytes which give the iris color.

- **Lens:** it is a transparent biconvex structure, very rich in beta-crystallins proteins (35%) which change with age contributing to lens opacity (cataract). The metabolism of the lens is mainly anaerobic, glucose and nutrients from aqueous humour. The lens is composed of six layers from anterior to posterior: anterior capsule, anterior epithelium, anterior cortex, central nucleus, posterior cortex and posterior capsule. The lens is held to the ciliary body by threads like called the zonules. The lens aids in bending the light towards the retina and capable of adjusting its refractive power so as to direct the light on the central vision area of the retina (fovea).

- **The ciliary body:** It is a muscular structure which extends from the end of the retina (ora serrata) till the scleral spur. The ciliary processes of the epithelium secrete the aqueous humour (clear fluid) into the posterior chamber (space between the iris and the lens). The aqueous humour is mostly composed of glucose (almost two thirds), protein, lactose and chloride. It is the main metabolic supply for the cornea and lens (avascular structures). The aqueous humour flows from the posterior chamber through the pupil to the anterior chamber angle (corneal-iris junction). The anterior chamber is the space between the iris posteriorly and the cornea anteriorly. The ciliary muscle applies forces on the sclera to facilitate the drainage of the aqueous humour through a canal known as the canal of schlemn at the iris-corneal angle to be drained in the venous system. Any defect that hinders drainage of the fluid results in accumulation of the fluid in the eye which ends up with increased intra-ocular pressure (basic glaucoma pathology).

- **Retina:** the most inner layer of the eye, facing the vitreous. It is the "screen" on which an image is formed by light that has passed into the eye via the cornea, aqueous humour, pupil, lens and finally the vitreous humour before reaching the retina. It consists of two basic layers:

1- **The neural retina:** This is the inner layer, it is made of nine layers most importantly the photoreceptor layer. Photoreceptors (sensory retina) contain the sensory cones which are responsible for color vision, detailed vision and the daytime vision, they are highly concentrated at the fovea (macular area). The sensory rods are responsible for night vision (black and white) and mostly

concentrated in the whole retina except the fovea. Photoreceptors convert the light they detect into nerve impulses that are sent to the brain along the optic nerve.

2- **The retinal pigment epithelium (RPE**): This forms the outer layer of the retina. It is a vascular structure which provides metabolic and functional support to the photoreceptors. Hence, it can contribute to pathologic processes of the whole retina including the sensory cells due to the leakage and obstruction of the vascular system. Retinal detachment is a serious retinal condition which characterised by separation of the sensory retina from the RPE. In general, retinal pathology (e.g retinopathy) ends up with visual disturbances due to death of the retinal sensory tissue as a result of malfunction and pathological RPE.

- **The vitreous:** The largest chamber of the eye (4.5ml), transparent gel composed of thin collagen fibres in a highly dilute solution of salts, proteins and hyaluronic acid (99% water). It assists in maintaining the eye shape and supporting the retina. The vitreous gets opaque mostly in association with retinal diseases like retinopathy due to blood leaking into it.

- **The optic nerve:** Is formed by the axons of the 1.2 million ganglion cells coming out from the retinal sensory cells. It also contains within its fibres the central retinal artery and the central retinal vein which emerge from the optic nerve head (optic disc or blind spot). The optic disc is a major ophthalmoscopic landmark of the ocular fundus; its color, the margins, the cup to disc ratio and the neuroretinal rim are all features for many pathological presentations like glaucoma. The optic nerve connects the retina with the brain. It is a transmitter of light impulses to the brain.

- **The choroid:** it is a vascular sheet, lying between the sclera and the retina. The outer vascular bed have large vessels, the inner bed consists of an extensive network of fenestrated vessels-the choriocapillaris- which is the major blood supply to the outer layers of the retina and to the whole macula including the fovea (central vision area).

3.4 Main diabetic eye diseases

Diabetes mellitus has been shown to affect nearly all the ocular tissue. However, significant visual loss can occur when retinopathy, cataract and glaucoma develop. All of which are leading causes of visual impairment associated with long standing diabetes mellitus. Nonetheless, optic neuropathy, corneal opacities, retinal detachment, vitreous opacities and retinal vascular occlusions have also been found to be associated with diabetes mellitus. Additionally, diabetes has been found to cause ocular and facial nerve palsies. This results in ocular mobility limitations and sometimes double vision (Jeganathan et al, 2008). Following is a detailed description of the main diabetic eye diseases:

3.4.1 Diabetic retinopathy:

Diabetic retinopathy is an eye disease characterised by damage of the retinal tissue that is associated with long-standing diabetes, (Kanski, 2003).

3.4.1.1 Etiology of diabetic retinopathy:

Prolonged periods of high blood sugar levels cause damage to the small blood vessels in the retina, mainly its' walls. The Pericytes which represent the vessels' barrier prevent leakage of blood contents out of the vessels to the retinal structure. Among diabetics, retinal vessels initially become leaky and then may block off due to loss of the Pericytes. This causes haemorrhages (spots of blood) and exudates (proteins and lipids) in the retina. The damaged vessels (hardening, narrowing, leaky, blocked), deformation of red blood cells and platelets aggregation can result in lack of oxygen and consequently ischemia of the retinal tissue. Later, as a response to ischemia, the growth hormones become active which initiate growth of new abnormal fragile vessels on the retina (neovascularization). These vessels tend to exacerbate further bleeding and result in more damage to the retinal tissue. As shown in figure (3.2), the marked difference between the healthy retina and retinopathy is the abnormal retinal haemorrhages and retinal aneurysms (USA-National Library of Medicine**,** 2007). Hence, the retina loses its function as a sensory organ to the light waves and as a transmitter of light impulses to the brain (Kanski, 2003).

3.4.1.2 Stages of diabetic retinopathy:

Diabetic retinopathy is of gradual onset, it progresses into different stages over time. Following is a description of each of these stages as described by (Kanski, 2003),

- **Background diabetic retinopathy:** represented in microaneurysms and microvascular occlusion (dot and blot heamorrhages) of the retinal vessels. Hard exudates (fat deposit), haemorrhages and retinal oedema are the main clinical findings of background diabetic retinopathy. Treatment in this stage involves periodic fundus examination (visualization of the retina through dilated eye pupils) to assess retinal prognosis and better control of blood glucose levels and hypertension.

- **Pre-proliferative diabetic retinopathy:** consists of vascular changes, cotton wool spots (ischemic nerve fibres), dark blot heamorrhages and intra-retinal microvascular abnormalities (IRMA) of the retina. It is a warning sign of progressive retinopathy. Laser treatment might be needed in this stage. However, better control of blood glucose levels is must.

- **Proliferative diabetic retinopathy:** formation of new fragile vessels on the retina (NVE) or at the optic disc (NVD). These abnormal vessels usually tend to

exacerbate retinal bleeding and tissue damage. They are further responsible for retinal ischemia, retinal detachment and vitreous opacity. Laser treatment is strongly recommended in this stage.

- **Maculopathy:** involvement of the fovea (part of retina that is responsible for the detailed vision) by oedema or hard exudates and bleeding. It is the most common cause of visual impairment in diabetic retinopathy. Management of maculopathy involves preventive measures like better control of blood glucose level and associated risk factors. Laser treatment is indicated under certain conditions.

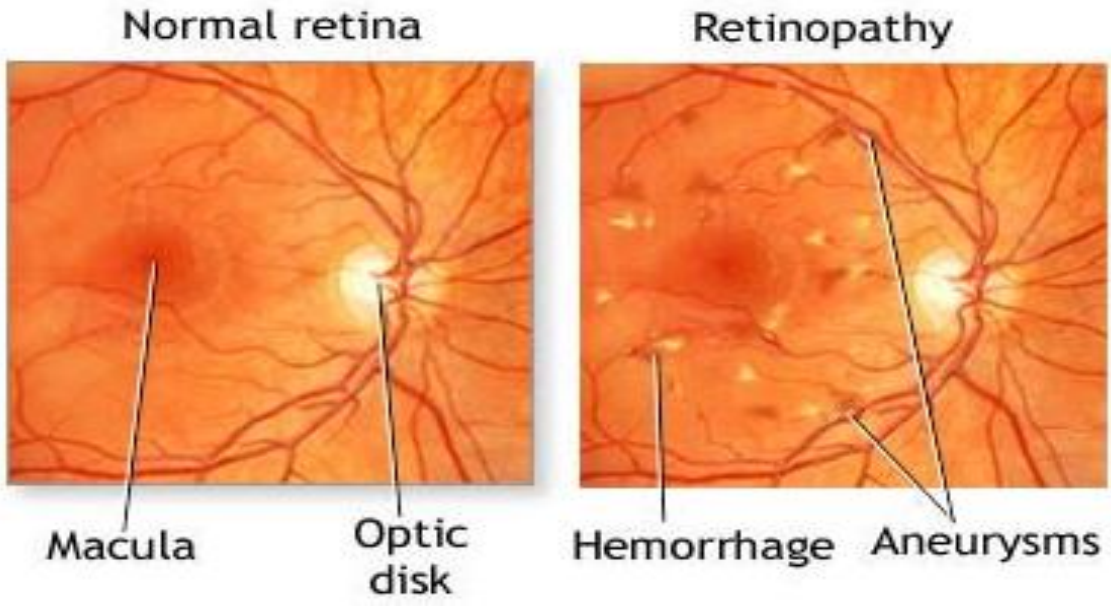

Figure (3.2): Normal retina and retinopathy.

3.4.1.3 Risk factors for diabetic retinopathy:

Following is a summary of the main prominent retinopathy risk factors,

Duration of diabetes: It is the most important factor. Duration of diabetes is the best predictor of the incidence and progression of the disease. Moreover, it is the marker for all diabetic chronic complications. The longer a person has diabetes, the greater the chance of retinopathy. However, in patients having type 2 diabetes, duration of the disease is usually inaccurate. Hence some patients at the time of presentation would have retinopathy indicating a lag time between the onset of the disease and clinical diagnosis (Negi and Vernon, 2003). Additionally, in both types of diabetes, retinopathy was found to be associated with increased duration of diabetes. After 20 years of diabetes, type 1 patients had proliferative retinopathy

(53%) more frequently than in type 2 diabetes patients (22%), (Klein BE and Klein R, 2006). This might explain the reason why diabetic retinopathy is commoner in type 1 than in type 2 diabetes mellitus patients. With type 1 diabetes, patients are exposed to longer duration of uncontrolled blood glucose and other risk factors more than type 2 diabetes. Twenty years after the onset of diabetes, almost all patients with type 1 diabetes and over 60% of type 2 diabetes patients will have some degree of retinopathy (Watkins, 2003). Furthermore, Klein and Klein R found that the level of glycosylated haemoglobin in each quartile was associated with the progression and incidence of retinopathy for the two types of diabetes (Klein BE and Klein R, 2006).

Age: Diabetic retinopathy was found to be positively associated with increased age. However, the relationship between retinopathy and age is more likely to be due to an association of retinopathy with duration of diabetes. Longer diabetes duration proceeds alongside increasing in age, and hence more exposure to diabetic effects. On the other hand, puberty which is related to age is another particular factor that is believed to have an effect on retinopathy. Before the age of 13 years old (before puberty), retinopathy is very uncommon regardless of duration of diabetes (Johnson et al, 1998)**.** However, age was found to be a risk factor for retinopathy regardless of the presence of other several retinopathy risk factors like duration, HbA1c and type of diabetes (Klein BE and Klein R, 2006).

Blood Sugar Control: Hyperglycemia is the main pathological basis for diabetes. Both observational and clinical studies have found a very strong relationship between the severity of retinopathy and uncontrolled blood sugar. Uncontrolled blood glucose levels tend to damage both large and tiny blood vessels which eventually induce retinopathy. However, good metabolic control will not prevent retinopathy development, actually, it hinders the disease progression. The United Kingdom Prospective Diabetes Study (UKPDS), one of the largest clinical research studies of diabetes (5102 type 2 diabetic patients followed-up for a median time of 11 years) provided conclusive evidence that retinopathy among type 2 diabetes patients can be significantly reduced through appropriate better blood glucose control. It was found that for every 1% increase in HbA1c, microvascular complications (including retinopathy) increased by 37% (Negi and Vernon, 2003). Additionally, the relationship between retinopathy and HbA1c was found at any stage of retinopathy (before proliferative stage) and at any duration of diabetes indicating the destructive role of uncontrolled blood glucose on retinopathy progression. This means that lowering blood glucose level at any duration time or before the retinopathy become advanced (end-stage proliferative) would lower the risk of retinopathy (Klein BE and Klein R, 2006).

Hypertension: High blood pressure increases the risk of eye diseases due to its effect on blood flow. It leads to weakening of the vessels, atherosclerosis (thickening of arterial wall) and rupture of vessels (stroke). Hypertensive retinopathy which is characterized by damage to retinal vessels and tissue ischemia is a retinal disease associated with hypertension even in patients without diabetes.

Hence, the effect of hypertension on the retina is exacerbated in association with diabetes mellitus. The United Kingdom Prospective Diabetes Study (UKPDS), found that tight blood pressure (mean blood pressure levels of 144/82 mm Hg) reduced the risk of retinopathy progression by 34%. When hypertension and diabetes occur together, both hypertension and hyperglycaemia should be vigorously treated so to limit the development of retinopathy, (Matthews et al, 2004, Genuth et al, 2002).

The association between hypertension and diabetic retinopathy has been documented by several studies, (Haddad and Saad, 1998, Tapp et al, 2003). However**,** Klein BE and Klein R reported that hypertension was not found related to retinopathy in type 2 diabetes, while it was for type 1 diabetes. This was suggested due to the protective effects of antihypertensive drugs (rennin-angiotensin) among type two diabetic patients which are believed to protect the retinal vascular system (Klein BE and Klein R, 2006).

Pregnancy: It was reported that pregnancy increases the rate of progression of retinopathy (Johnson et al, 1998, Kanski, 2003).

Other risk factors: inconsistent findings regarding the association between retinopathy and alcohol drinking, obesity, gender, physical exercise and socio-economic status were found among different groups by different investigators (Johnson et al, 1998, Negi and Vernon, 2003).

3.4.1.4 Visual impairment associated with diabetic retinopathy:

Retinopathy could be asymptomatic in its early stages; patients might not develop visual disturbances. However, fluctuation of visual disturbances is common among diabetics due to retinal and macular oedema which is associated with uncontrolled blood glucose levels. When improvement in blood glucose levels takes place, oedema resolves and hence patients restore vision. However, in advanced maculopathy, the central vision area (fovea) loses its function due to the tissue damage; the result is severe irreversible visual loss. With advanced retinopathy, ischemic changes of the whole retinal structure and sensory cells result in permanent loss of vision according to the extent of tissue damage. Retinopathy induces damage to the nerve tissue; hence the light signals can not be transmitted to the brain for interpretation. Additionally, haemorrhage which is associated with retinopathy would extend to the clear vitreous gel making it opaque. This will obstruct the light coming from the anterior part of the eye to reach the retinal sensory cells which eventually induces visual loss. Finally, in advance diabetic retinopathy, the sensory retina tends to get detached from the underlying support structure, the result is loss of vision, (Johnson et al, 1998)**.**

3.4.2 Cataract:

Cataract is a clouding of the eye's natural lens which obstructs the passage of light towards the inner eye structures. Lens opacity can be as a result of different risk factors and causes involving different mechanisms. While cataract could be congenital, it could be also due to lens trauma, toxic substances and associated with systemic diseases. However, age related cataract (senile cataract) is the most common type and develops alongside the aging process (Kanski, 2003). Please see figure (3.3) which shows the difference between the transparent lens and cataract (Feinberg, 2006).

3.4.2.1 Etiology of diabetic cataract:

The changes in the lens protein metabolism and capsules as a result of aging remain the leading cause of cataract formation. The pathophysiology behind senile cataracts (age-related) is complex and not fully understood. It is multi-factorial involving complex interactions between various physiologic processes. As the lens ages, its weight and thickness increases, new cortical layers are added. The central nucleus is compressed and hardened in a process called nuclear sclerosis. Changes of the lens epithelium result in an alteration of lens fiber formation and homeostasis. The result is loss of lens transparency. Furthermore, as the lens ages, a decrease in the rate of transport of water, nutrients, and antioxidants leads to lens opacity. Other areas being investigated include the role of nutrition in cataract development, particularly the involvement of glucose, minerals and vitamins (Ocampo, 2008). However, the biological mechanism whereby high glucose levels lead to cataract is not clear. It is believed that diabetes results in elevated levels of glucose in the lens. Glucose then reduced to sorbitol (sugar) which is hardly excreted from the body tissue. High levels of sorbitol in the eye lens damages the lens protein and eventually loss of lens transparency (cataract). Moreover, the oxidative damage to membrane lipids of the lens as a result of high blood glucose has been postulated to have an effect on cataract formation among diabetics (Rowe et al, 2000). On the other hand, it is evident that over-hydration of the eye lens (snow-flecks cataract) which is associated with diabetes mellitus remains a main cause of visual disturbances among diabetics (Johnson et al, 1998). Seddon et al found that cortical and posterior subcapsular cataracts were associated with diabetes (Seddon et al, 1995). Similarly, Mukesh BN et al, found that diabetes was an independent risk factor for posterior sub-capsular cataract (Mukesh et al, 2008).

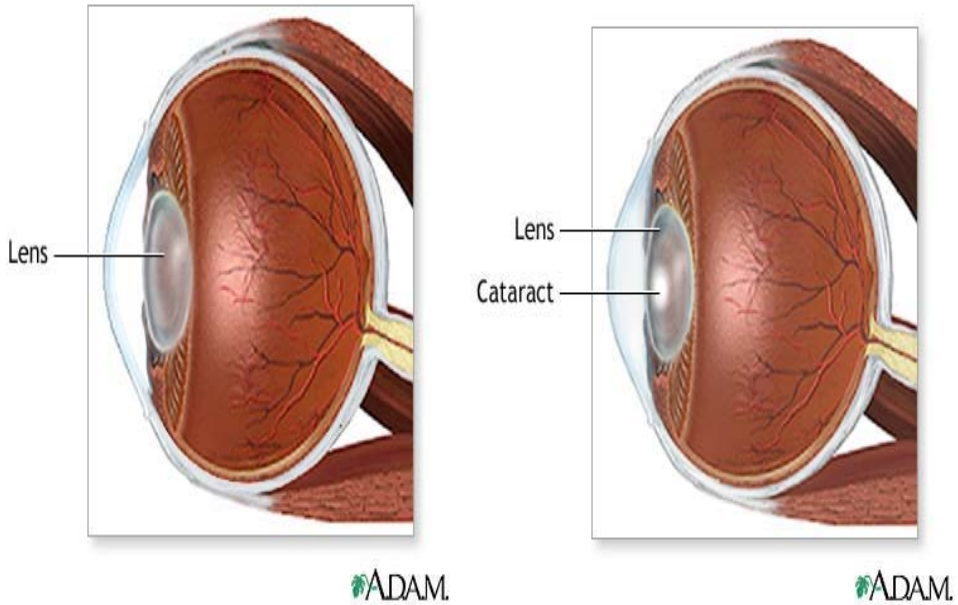

Figure (3.3): The difference between the transparent lens and cataract.

3.4.2.2 Main cataract classifications:

Following is the main classifications of cataract as abstracted by (Kanski, 2003)

- **Cortical cataract**: lens opacity forms in the lens cortex, gradually extends from the outside of the lens to the centre.
- **Nuclear cataract**: cataract forms in the nucleus (the centre of the lens) and then to the whole lens.
- **Capsular cataract:** opacity at the lens capsule, either the posterior or the anterior capsule.
- **Subcapsular Cataract:** opacity begins adjacent to the lens capsules.

3.4.2.3 Cataract risk factors:

Following are the main risk factors for cataract:

Identifying the risk factors responsible for cataract formation is difficult and complicated simply because a realistic causal model in cataract formation is not simple (one exposure-one cataract type). However, as mentioned earlier (3.5.2), the etiology of diabetes as a risk factor for cataract is not fully clear. Nevertheless, an association between diabetes and cataract has been documented in both hospital based studies and population based studies in a wide variety of populations. Hence, diabetic risk factors like blood glucose levels, hypertension, duration of diabetes

and age would eventually have an effect on cataract formation. However, inconsistent findings by different studies were reported; more details about epidemiological findings will be explored in literature review and discussion parts of the thesis. In spite of this, we will explore the most prominent cataract risk factors in the general population in order to give a better insight about the determinants of cataract:

Age: the strongest risk factor. Prevalence of cataract increases with age as found in the developed and developing countries (Johnson et al, 1998). Mukesh et al, found that increased age was a risk factor for the development of all types of cataract with an increasing risk trend throughout life for nuclear cataract (Mukesh et al, 2008). Additionally, in India, all types of cataract were found to be associated with increased age (Nirmalan et al, 2004). Nuclear cataract, cortical cataract and sub-capsular cataract were found to be associated with increasing age among diabetics (Klein BE and Klein R, 2006).

Gender: prevalence of cataract is higher in females than males. Numerous epidemiological studies have found that female gender is a risk factor for cataract. However, there is some evidence that the excess risk associated with being female, is more prominent for cortical rather than nuclear cataract or sub-capsular cataracts. Several case control studies have found that the excess risk for women persists after controlling for other risk factors. It is believed that productivity and female hormones play an effect (Johnson et al, 1998). Female sex, was found to be an independent risk factor for development of cortical cataract (Mukesh et al, 2008). Similarly, females were found more likely to have cortical cataracts and nuclear cataracts (Nirmalan et al, 2004).

Cigarette smoking: there is an increasing evidence for causal association between cigarette smoking and cataract formation. Such evidence was supported by eight studies (cohort, cross-sectional and case-control studies) in different populations. Consistent findings have shown that smoking is a risk factor for nuclear and posterior sub-capsular cataract. However, smoking was not related to cortical cataract (Mukesh et al, 2008, Seddon et al, 1995).

Sunlight: It was found by several studies that exposure to sunlight, specifically ultra-violent light, is a risk factor for cortical and posterior sub-capsular cataract. However, confounding risk factors alongside sunlight is difficult to control. Hence, the results of these studies remain under critics. Cortical and posterior subcapsular cataracts appear to be related to environmental stresses such as ultraviolet exposure (Seddon et al, 1995).

Steroid therapy: it is one of the strongest known cataract risk factors for posterior sub-capsular cataract. Corticosteroids greatly affects adrenal gland and hence the salt-water movement in the tissue. It also affects blood glucose levels (Johnson et al, 1998). Cumming et al, found that even inhaled steroid therapy is a risk factor for cataract. Their findings revealed that there was a higher prevalence of nuclear cataracts among patients using inhaled steroids compared with non-users (relative

prevalence, 1.5:95). Similarly, posterior subcapsular cataracts was also higher among steroid users compared with non-users (relative prevalence, 1.9:95). However, there was no difference between the two groups in regard to cortical cataract (Cumming et al, 1997).

Hypertension: Inconsistent findings regarding the association between the two diseases (hypertension and cataract) was documented by several studies. While several epidemiological studies have found an association between the diseases, others did not report such association. However, the mechanism by which hypertension is a risk factor for cataract still unclear, nevertheless, it is possible that a certain mechanism related to the circulatory system may be involved (Johnson et al, 1998). One of the largest case-referent studies carried out in central India, attempted to include as many risk factors as possible to study their independent and joint contribution in the development of cataract. The study found that hypertension is a risk factor for cataract. Better control of blood pressure helps on the reduction of cataract (Ughade et al, 1998). Similarly, Nirmalan et al found that hypertension was a risk factor for cortical cataract development (Nirmalan et al, 2004).

Other risk factors: many different risk factors were reported to be associated with cataract. This includes alcohol, oestrogen, short sightness and low body mass. However, such risk factors are still classified as possible risk factors rather than strong ones (Johnson et al, 1998), (Nirmalan et al, 2004, Ughade et al, 1998).

3.4.2.4 Visual impairment associated with cataract:

Decreased visual acuity is the most common complaint of patients with cataract. Cataract is considered clinically relevant if visual acuity is affected significantly. Furthermore, different types of cataracts produce different effects on visual acuity. Mild degree of posterior subcapsular cataract can produce a severe reduction in visual acuity. However, nuclear cataract is usually associated with decreased distance acuity. Cortical cataract generally is not clinically relevant until the lens opacity extends to the visual axis (central part of the lens). The progression of cataract may increase the diopteric power of the lens resulting in a mild-to-moderate degree of myopia (short sightedness). On the other hand, cataract might lead to double vision due to the change in the refractive power in different locations of the lens, mainly in the lens nucleus. However, complete opacity of the lens will eventually lead to loss of vision until surgical removal of the eye lens. While cataract formation can not be prevented, however, some of its risk factors could be controlled (like diabetes mellitus) which in turn delay the onset of cataract formation and hence restore vision and minimize the need for cataract surgery (Allingham et al, 2005).

3.4.3 Glaucoma:

Glaucoma is of different types and classifications including primary, secondary, congenital, associated with systemic diseases and syndromes. It could be a result of drugs, trauma and idiopathic. Glaucoma is not merely a single disease; there are different pathophysiological mechanisms and clinical presentations for glaucoma. Therefore, there is no single definition that properly covers all forms of glaucoma. However, glaucoma is the term for a diverse group of eye diseases, all of which involve progressive damage to the optic nerve, increased intra-ocular pressure and loss of vision (partial or total), (Allingham et al, 2005, Johnson et al, 1998).

3.4.3.1 Etiology of glaucoma:

The increased fluid pressure inside the eye causes compression of the retina and the optic nerve (ganglion cells) which can eventually lead to nerve damage as shown in figure (3.4) (Subramanian, 2007). Optic nerve damage is characterized by paleness appearance, loss of tissue (cupping) and even loss of the optic nerve rim, all of which can be clinically visualized under magnification. Increased intra-ocular pressure could be of different causes. However, the main underlying causes are of two reasons, either an increase production of aqueous humour (fluid) by the ciliary body or decrease drainage of the fluid out of the eye (from the iris-corneal angle) to the vascular system. The normal intra-ocular pressure ranges between 12-22 mm/Hg. Nowadays, glaucoma features (optic nerve damage and visual loss) have been found even in the absence of increased intra-ocular pressure (normal tension glaucoma). Hence, recently increased intra-ocular pressure has been considered by many investigators as a risk factor for glaucoma. Therefore, the definition of glaucoma has changed radically since its identification. In this respect, the following paragraph will describe the two major glaucoma types that were found associated with diabetes and were intensively investigated by the literature (primary open-angle glaucoma and neovascular glaucoma), (Allingham et al, 2005).

3.4.3.2 Primary open-angle glaucoma (COAG):

Primary open angle glaucoma (POAG or COAG) is the most common form of the disease, it accounts for 60-70% of all glaucoma types. It is described as a multi-factorial optic neuropathy (loss of optic nerve fibers) that is chronic and progressive. Such loss develops in the presence of open anterior chamber angles (open drainage system), visual field abnormalities and increased intra-ocular pressure. More over, the disease might develop even in the absence of increased intra-ocular pressure (normal tension glaucoma). COAG manifests by cupping and atrophy of the optic disc. The disease is painless and hence permanent damage to the eye's optic nerve may not be noticed until severe visual loss develops. That is why the exact mechanism of COAG is not clear. However, it is believed that vascular dysfunction and compression of the optic nerve axons result in ischemia to the optic nerve. Such belief might explain the relationship between the disease and diabetes mellitus (Allingham et al, 2005). In Canada, it was found that open angle

glaucoma was found to be associated with diabetes (Perruccio et al, 2007). The main risk factors for COAG are as follows:

Age: In every populated study, prevalence of COAG was found to increase with increased age. However, the nature of eye changes related to age is not clearly understood. It is possible that successive episodes of optic nerve damage take place throughout life and become prominent by increasing age. As a rule of thumb, prevalence of glaucoma increases with increasing age, (Allingham et al, 2005, Allingham et al, 2005). In Canada, it was found that all forms of glaucoma were associated with increased age (Perruccio et al, 2007).

Myopia: short-sighted has been found to be a strong risk factor for open-angle glaucoma. Such association was found by numerous epidemiological studies, both case-control and population based studies. The Blue Mountain eye study has reported such association after adjustment to a number of glaucoma risk factors (Mitchell et al, 1999).

Race: The highest prevalence was found among black people and intermediate in white people. It is possible that black people have a higher skin pigmentation which eventually results in reduction of eye fluid outflow and then higher intra-ocular pressure. Additionally, genetic and nutritional factors might play an important role (Johnson et al, 1998), (Allingham et al, 2005).

Family history: A genetic factor may predispose to the development of COAG. The first degree relative with glaucoma has been consistently associated with an increased risk of the disease. A major gene known as OAG allele was found constantly associated with COAG (Johnson et al, 1998).

Diabetes mellitus: Prevalence of COAG appears to be higher in the diabetic population by a factor of about 2 as found by the majority of population-based surveys, (Mitchell et al, 1997), (Klein et al, 1994), (Chopra et al, 2008). However, Tielsch JM et al, did not find such association in their population-based study (Tielsch et al, 1995). The findings from numerous clinical studies are inconsistent regarding the association between the two diseases. This is mostly due to wide variations in methodological approaches (Ellis, et al, 2000).

Hypertension: Confusing findings were found regarding the association between glaucoma and hypertension as found by different studies. In Australia, hypertension was found to increase the risk of glaucoma (Mitchell et al, 2004). Furthermore, The Baltimore Eye Survey found that an increase in either systolic or diastolic blood pressure is associated with increased intra-ocular pressure. Whereas, a decrease in diastolic blood pressure below 50mm Hg was found to be associated with increased prevalence of open angle glaucoma On the other hand, increased systolic blood was associated with increasing the risk of open angle glaucoma (Tielsch, et al, 1995). However, it was found that increased in systolic blood pressure increased the risk of open angle glaucoma. While, both systolic and diastolic blood pressure were

associated with the main disease feature (increased intra ocular pressure) (Dielemans et al, 1996). Conversely, Leske et al did not find an association between either the systolic or diastolic blood pressure and glaucoma (Leske, 1995). On the other hand, it was found that younger hypertensive patients seem to be protected against developing COAG, while older in age have shown a double risk of developing the disease. Hence, age might be a confounder among hypertensive patients (Johnson et al, 1998).

3.4.3.3 Neovascular glaucoma:

The name of the disease came from the formation of new blood vessels (neovasularization) on the iris and adjacent tissue (rubeosis iridis) due to ischemia of the eye tissue, mainly the vascular structure of the eye. Most of cases are preceded by a hypoxic disease of the retina. Like other types of glaucoma, optic nerve damage and hence visual loss is an absolute result (Allingham et al, 2005). The main risk factors for neovascular glaucoma as abstracted by (Allingham et al, 2005) are as follows:

Retinopathy: Profound retinal ischaemia that is associated with advanced retinopathy stimulates production of vascular endothelial growth factor, which diffuses into the anterior segment of the eye and causes neovascularization of the iris. Approximately one third of rubeosis iridis (neovasularization) have diabetic retinopathy. The occurrence of rubeosis iridis and hence neovascular glaucoma increased dramatically after vitrectomy surgery (surgical treatment of retinopathy). Proliferative diabetic retinopathy remains a leading cause of neovascular glaucoma, second only to central retinal vein occlusion (Negi and Vernon, 2003).

Retinal vascular occlusions, vein and artery: Diabetes mellitus and hypertension are main predisposing factors for retinal vascular occlusions. Retinal vascular occlusions induces hypoxia and then growth of fragile vessels on the iris (neovasularization). The result is neovascular glaucoma (Johnson et al, 1998), (Negi and Vernon, 2003).

Other risk factors: Any disease which might induce retinal hypoxia including retinal detachment, inflammatory diseases and Choroidal melanomas could rise to neovascular glaucoma (Johnson et al, 1998, Negi and Vernon, 2003).

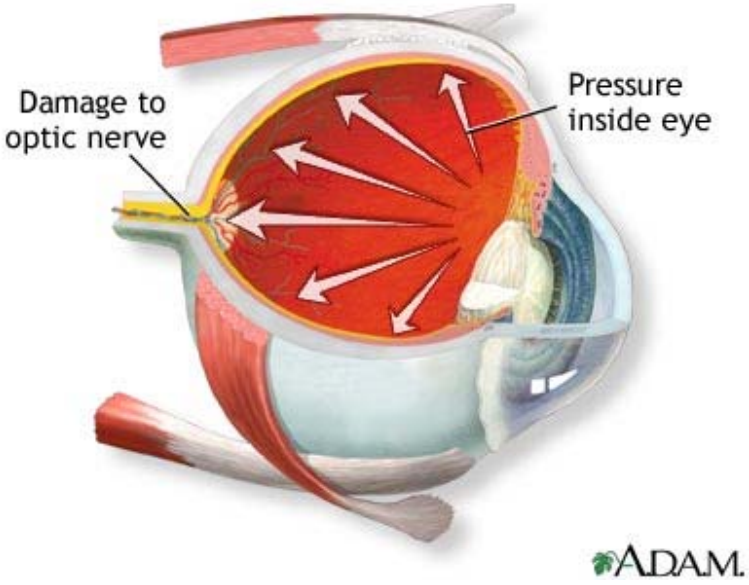

Figure (3.4): Etiological mechanism of glaucoma

3.4.3.4 Visual impairment associated with glaucoma:

Glaucoma can cause partial vision loss and eventually blindness according to the extent of damage to the neural cells, mainly the optic nerve. Optic nerve damage produces certain characteristic visual field defects in the individual's peripheral (side) vision as well as central vision. Patients with glaucoma, mostly chronic open angle glaucoma don't know they have it. Hence, gradual and incipient loss of peripheral vision is common. If the IOP remains high, the destruction can progress until tunnel vision develops. This means that patients lose their peripheral vision where only central vision (macula-fovea) remains active for a while; ability to see only objects that are straight ahead. In late stages of the disease, central vision is also destroyed where total blindness is the end result of glaucoma. Loss of vision due to glaucoma is irreversible and can not be restored back similar to that induced by retinopathy. This is due to ischemia of neural tissue. Therefore, the importance of protective measures through prevention, early detection and treatment is crucial (Kanski, 2003).

3.5 WHO definition of visual impairment

According to Johnson et al, visual status as defined by WHO is of the following categories (Johnson et al, 1998),

- **Normal and Functionally accepted vision**: visual acuity of no less than 6/18 in the better eye with best possible correction (VA≥ 6/18).

- **Visual impairment is Low vision and Blindness:**

I. **Low vision:** visual acuity of less than 6/18 but equal to or better than 3/60 in the better eye with best possible correction (6/18>VA ≥ 3/60).

II. **Blindness**: visual acuity of less than 3/60 in the better eye with best possible correction, or a visual field loss in each eye to less than 10º from fixation (VA<3/60).

In visual acuity testing, the C chart should be adequately illuminated. Each eye is tested separately. In the presence of more than one cause of visual impairment in the same eye, for example, cataract and severe glaucoma, a clinical judgment must be made to decide which disease contributing most to the visual impairment. The convention adopted by World Health Organization is that the cause in the individual should be the one most easily preventable or curable so as to make the person non-visually impaired. It is valuable then to list those exclusive and combined causes of visual impairment in identifying the contribution of each disease to visual impairment.

3.6 Conceptual frame work

The conceptual frame, as explained in (figure 3.5), shows the overall concept of diabetic eye risk factors and eye complications:

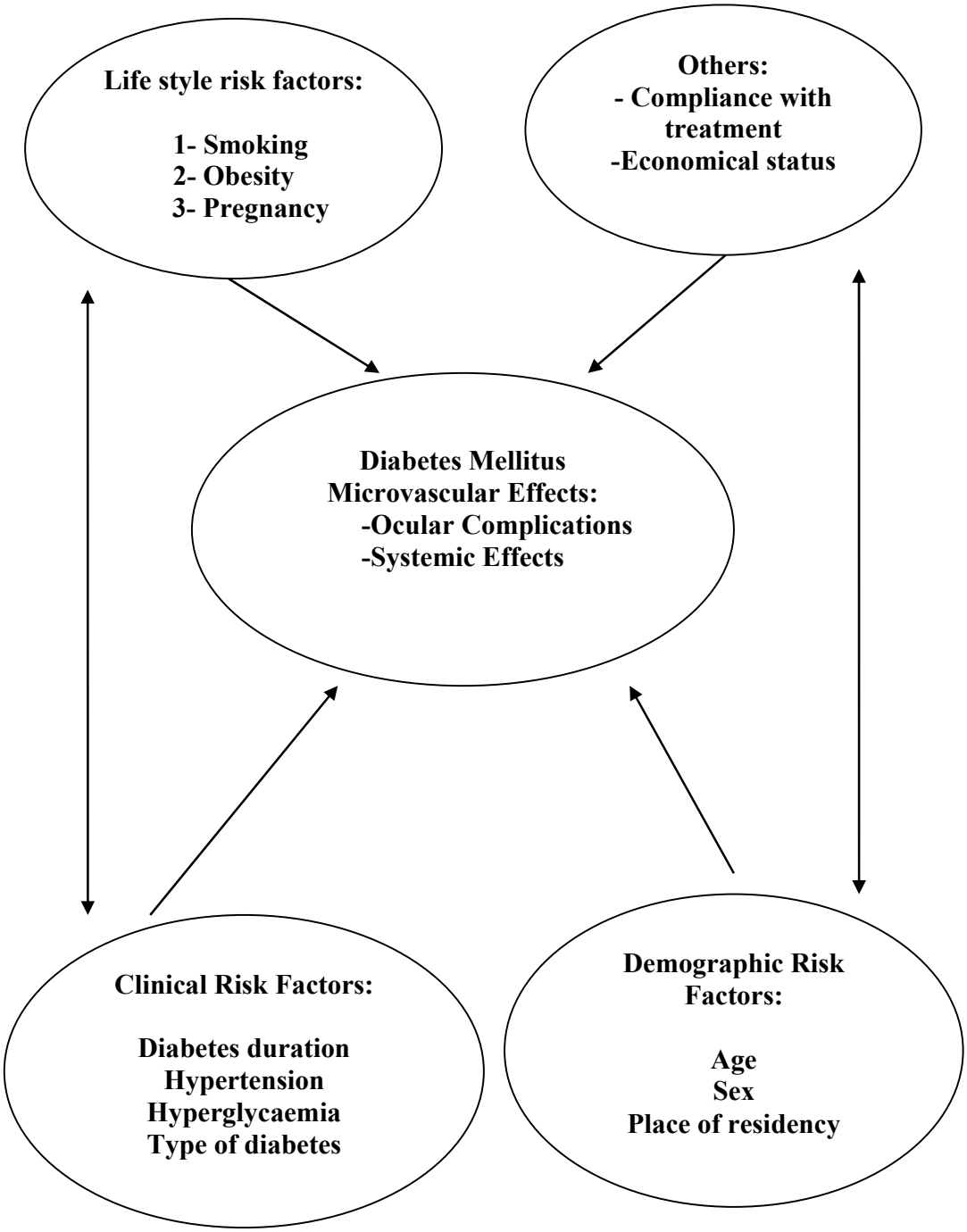

Figure (3.5): conceptual frame work

Chapter Four. Study Methodology

4.1 Introduction

4.2 The study geographical settings; St. John Eye Hospital community settings

4.3 Study design

4.4 Study sample method and size

4.5 Data collection instruments

4.6 Operational definition of variable

4.7 Pilot testing

4.8 Data Analysis

4.9 Study ethical approval and considerations

4.10 Chapter Summary

4.1 Introduction

The emphasis of this study was on identifying the percentages of the main diabetic eye complications and related visual impairment among the study sample. Additionally, to estimate the effect of selected diabetic eye risk factors on both diabetic eye complications and visual impairment. In this chapter, the study geographical settings, design, and the sampling method are explained. The study data collection tools and instrumentations are also described. Finally, data analysis, pilot testing and the study ethical considerations are clarified. -

4.2 The study geographical settings; St. John Eye Hospital community settings

The study was conducted on a sample of diabetic patients who were screened and treated by St. John Eye Hospital community settings (St John Hebron Eye Center and St John Outreach mobile Eye clinic). The study geographical background is the whole West Bank districts regardless of the residents' sex, religion and health status. The present study setting "St John West Bank community settings" consists of:

1-St. John Hebron Center: It was opened in November 2005. It operates an outpatients' department which provides general eye care, pediatric orthoptic assessment and diabetic eye care. It opens five days a week. The center performs a day case cataract surgery once a week, with a weekly average of 8 cataract surgeries. The center is one of the main eye care settings for Hebron district residents. Diabetic eye care is one of the prominent ophthalmic services at the center. Diabetic eye screening, diagnostic services, laser treatment and health education are all available. The center is the main referral for the governmental and UNRWA patients through different agreement conditions with both bodies (St. John Eye Hospital, 2007).

2- Outreach Mobile eye clinic: It primarily provides primary and secondary eye care throughout the West Bank. While it provides general eye screening sessions, at least two diabetic screening sessions being held weekly in different West Bank districts. Laser treatment for diabetics being provided in the community during the screening sessions. The program is totally free of charge. The Outreach mobile clinic screen and treat a yearly average of 5500 patients. Among the total around 20% are diabetics. The outreach mobile clinic implement its services in coordination with community partners like non-governmental organizations, health care centers, charitable institutions and governmental clinics. Palestinian medical relief, Union of health care committee, Palestinian Red Crescent Society, United Nations clinics and the Governmental community clinics are all outreach partners. The role of the partner is to provide the place for clinical examination and to book patients from the local communities for screening. Usually, those diabetic patients being followed up by the community partners for general diabetic care are referred to the outreach mobile clinic for eye screening. Diabetic patients who need further interventions (therapeutic or diagnostic) are referred to the base hospital in Jerusalem, (St. John Eye Hospital, 2007)

The investigator has excluded diabetic patients from the base hospital in Jerusalem because most of the hospital attendants are referrals from the hospital community settings (Hebron Centre and the Outreach Mobile eye clinic). Further more, the base hospital mostly provides advanced diabetic retinal and eye care rather than screening. Moreover, in the last few years, Jerusalem has become hardly accessible for West Bankers due to political reasons. The aim was to have the best possible homogeneous sample of patients. Finally, the computer coding system at the base hospital in Jerusalem does not give "diabetes" a computer code. Hence, it was difficult to catch up with all diabetic patients and to recollect their medical records.

4.3 Study design

A cross-sectional study was conducted to meet the study objectives. Patients' medical records were used to abstract the relevant data.

4.4 Study sample method and size

To better suits the study restricted time frame, a random sample of three months period (1st January 2007 – 31 March 2007) was selected to represent the whole year of 2007. The medical files of 420 diabetic patients (having type 1 and type 2 diabetes) who were screened and treated by St John Hebron Center (99 patients) and St John Outreach clinic (321patients) between 1st January 2007 – 31 March 2007 were included in the study. Diabetic patients who were found on diet (6 patients) were excluded from the study. This is because their diabetic status in terms of diagnosis was not confirmed and would have shown different metabolic characteristics. Two more patients who were found having a previous history of eye traumas with visual impairment were also excluded from the study.

4.5 Data collection instruments

To better organize and collect data from the patients' medical records, a data collection sheet was devised according to the related and needed information. The main features of the sheet include the patient's personal data, visual status and causes of visual impairment; such information being routinely recorded and documented in the patients' medical records by the medical and para-medical staff. Please see appendix (1) which shows the detailed data collection sheet items.

All patients were assessed by St. John Eye Hospital community settings (St John Hebron Eye Center and St John Outreach mobile Eye clinic) medical and

paramedical staff. The assessment included detailed medical history and examination. Patients' personal details, chief eye complains, medical and surgical ophthalmic and general health history were taken by specialized ophthalmic nurses. Best corrected visual acuity was measured by the specialized ophthalmic nurses using the standard Snellen chart. Patients underwent full slit lamp clinical examination by the ophthalmologists. Clinical eye examination included anterior eye segment assessment (orbital structure, cornea, iris, anterior chamber and lens) and tonometry (measurement of intra-ocular pressure using applanation tonometry). Posterior segment examination (Funduscopy) which included vitreous, retinal and optic nerve assessment was part of assessment. Funduscopy was done through dilated eye pupils using a slit lamp and magnifying lenses. All information and findings were documented in the patients' individual medical records. All related information was transferred from patients' medical records to the data collection sheet by the researcher himself. Please see Appendix (2) which describes St. John eye hospital data collection instruments and tools.

4.6 Operational definition of variables

1 - Dependant variables of diabetic eye complications:

Diabetic retinopathy: diagnosis of retinopathy of any stage that was made and documented in the patients' individual medical records.

Cataract: diagnosis of cataract of any type that was made and documented in the patients' individual medical records.

Glaucoma: diagnosis of glaucoma of any type that was made and documented in the patients' individual medical records.

Diabetic eye co- morbidities: diagnosis of retinal detachment, vascular retinal occlusion, corneal opacities and others (posterior lens capsule opacity, retinal diseases, squint, uveitis, pterygium and surgical complications) that were made and documented in the patients' individual medical records.

Visual impairment according to WHO definition: Low vision and blindness:

The results of the participants' visual acuity measurement that were documented in the patients' medical records were categorised as follows:

A- Normal and functional vision: visual acuity of no less than 6/18, in the better eye with best possible correction (functional vision=VA $\geq$ 6/18).

B-Visual impairment is Low vision and Blindness:

I-Low vision: defined as visual acuity of less than 6/18, but equal to or better than 3/60, in the better eye with best possible correction (low vision = 6/18>VA $\geq$3/60).

II-Blindness: defined as visual acuity of less than 3/60 in the better eye with Best possible correction- (Blindness=VA<3/60).

2- Independent variables of diabetic eye complications:

Personal characteristics and socio-economical factors: Participants' characteristics that had been documented in the patients medical records;

Age: the number of years a patient has lived at the time of eye examination by St. John eye hospital settings (rounded to the nearest year) that was reported by the patient and documented in his/her medical record. Age was categorised into quartiles: (1^{st} quartile 30-52 years), (2^{nd} quartile 53-59 years), (3^{rd} quartile 60-65 years), (4^{th} quartile 66-87years).

Sex: the gender of the patient either male or female that was documented in the patients' individual medical records.

Address: the reported place of residency (district) at the time of eye examination by St. John eye hospital settings and documented in his/her medical records (Hebron, Bethlehem, Ramallah, Jericho, Nablus, Salfeet, Tulkarem, Qalqelieh and Jenin).

Diabetes mellitus: type of diabetes mellitus the patient reported to have. Either type I diabetes or type II diabetes and having treatment (diabetic tablets, insulin or both at the time of examination) that was documented in the patients' individual medical records.

Duration of diabetes: the number of years the patient had reported having diabetes mellitus at the time of examination by St John eye hospital facilities (rounded to the nearest year); categories (0-5 years), (6-10years), (11-15 years), (16-60years).

Glycosylated haemoglobin (HbA1c): the reading value of the patients' Glycosylated haemoglobin (HbA1c) that was documented in the patients' individual medical records or either reported by patients or a laboratory test results form. Quartile categories (1^{st} quartile 4.5-7), (2^{nd} quartile 7.1-8), (3^{rd} quartile 8.1-9.1), (4^{th} quartile 9.2-13.2).

Hypertension: any patient previously diagnosed with hypertension and on anti-hypertensive medication that was reported by the patient and documented in the patients' individual medical records.

Clinical settings: the St. John health care facility by which the study participants were seen and screened;

1- St John Hebron eye clinic

2- St John outreach mobile eye clinic.

4.7 Pilot testing

A pilot test was done so as to ensure the compatibility between the collected data and related instruments and the study objectives. Those patients who were screened during the first two weeks of December 2006 (78 patients) were purposively chosen for analysis testing. The pilot study has found out that there should be an amendment in the SPSS coding categories for the causes of visual impairment. For those patients who have had mature cataract or corneal opacities (opaque media), visualization of the retina was not possible. So, making diagnosis regarding diabetic retinopathy could not be possible. An additional category of "No fundus view" was added to the causes of visual impairment to match clinical diagnosis and SPSS coding.

4.8 Data Analysis

The collected data was coded and entered into the computer using the Statistical Package for Social Sciences-software version 13 (SPSS) for analysis. Both descriptive and inferential statistics were used in data analysis. Data analysis was conducted in the following manner:

1-We calculated the frequencies and percentages of participants' general characteristics, clinical characteristics, diabetic eye diseases and all other independent variables.

2-Cross tabulations of the diabetic eye risk factors and diabetic eye complications were done. The chi-square test was used to determine the relationship between diabetic eye risk factors and diabetic eye complications. Binary logistic regression analysis was performed to estimate the odds ratios (expected B) for each of the study independent variables (unadjusted OR). To check for confounding and interaction among the independent variables, all of them were re-entered in the model (enter-mode) to examine the value change and direction of OR (adjusted OR). Confidence interval for expected (B) was calculated (95%CI).

3-Cross tabulations of the diabetic eye risk factors and visual outcomes were also done. The chi-square test was used to determine the relationship between diabetic eye risk factors and visual outcomes. Binary logistic regression analysis was performed to estimate the odds ratios (expected B) for each of the study independent variables (unadjusted OR). To check for confounding and interaction among the independent variables, all of them were re-entered in the model (enter-mode) to examine the value and direction of OR (adjusted OR). Confidence interval for expected (B) was calculated (95%CI).

4- Independent samples T-test was used to calculate the difference in mean values for age, duration of diabetes, HBA1c and first time eyes were checked for patients with diabetic eye complications compared to those without complications.

5-For all analysis, a p value of ≤ 0.05 was considered statistically significant.

4.9 Study ethical approval and considerations

Ethically, the research various phases are neither experimental nor invasive in nature, where by either way it would not harm the study participants either physically or psychologically. No doubt that any research paper that would be conducted to estimate and find out the burden of eye diseases in the Palestinian community would bring about- at the end of the day- the most appropriate and cost effective medical care at all levels of preventions. In addition, such research paper would underpin the future wider scale papers. Prior commencing the study- the study proposal phase- the investigator obtained the approval and support from the hospital ethical committee whereby the hospital medical records could be used for the study purpose and objectives. Please see appendix (3) which shows the study approval form that was signed by the hospital Research Ethical Committee.

4.10 Chapter Summary

This study is cross-sectional, with an overall aim of calculating the frequencies of diabetic eye complications and visual impairment among 420 diabetic patients. The impact of diabetic eye risk factors on diabetic eye complications and visual impairment was estimated. The study gathering tools and instruments that were used in data collection were explained. Descriptive statistics was used in data analysis. Univariate and Bivariate analysis was done to compare the relationship between the dependant and independent variables.

Chapter Five. Results

5.1 Introduction

In this chapter, the results of the study are presented. A total of 420 patients were included in this study; all of which were evaluated for the presence of diabetic eye complications and related visual impairment. Prevalence of diabetic eye complications was calculated as percentages of the total study participants stratified by sex, type of diabetes mellitus, clinical settings, HbA1c quartile categories, duration of diabetes mellitus quartile categories and hypertension status. Data analysis progresses from describing the study participants' general and clinical characteristics in terms of frequencies of the independent and dependent variables. Furthermore, the association between dependent (diabetic complications and related visual impairment) and independent variables (gender, type of diabetes mellitus, HBA1c, hypertension, clinical setting, duration of diabetes mellitus and age) was presented and described. Confidence interval at 95% and p value ≤ 0.05 were considered significant.

5.2 Participants' general characteristics

In table (5.1), the general characteristics of the study participants are presented. As the table depicts, out of the total participants (n=420), the majority of patients 76.4% (n=321) were screened by the mobile outreach clinic, whereas 23.6% (n=99) of patients were seen by Hebron clinic. The distribution of male patients was 41.7% (n=175) while the rest of the participants 58.3% (n=245) were females. Age groups are presented as quartiles. The mean age (SD) of the participants was 58.64 (9.3) years. The majority of patients 30% (n=126) were from Hebron district versus 5.2% (n=22) who were from Salfeet district- the least number of patients among the districts.

Table 5.1: General characteristics of the study participants

	Salfeet Class	5.2 (22)
Clinical Setting	Outreach clinic	76.4 (321)
	Hebron Clinic	23.6 (99)
Gender	Male	41.7 (175)
	Female	58.3 (245)
Age group/ years	30-52	25.2 (106)
	53-59	25.0 (105)
	60-65	26.2 (110)
	66-87	23.6 (99)
District	Hebron	30.0 (126)
	Bethlehem	9.0 (38)
	Ramallah	15.0 (63)
	Jericho	6.2 (26)
	Nablus	12.1 (51)
	Tulkarem	6.7 (28)
	Qalqelieh	6.7 (28)
	Jenin	9.0 (38)

5.3 Participants' clinical characteristics

Table (5.2) summarizes the participants' clinical characteristics in relation to type of diabetes, hypertension, duration of diabetes and HbA1c. Most of the study participants 95.2% (n=400) had type 2 diabetes mellitus compared with only 4.8% (n=20) who had type 1 diabetes mellitus. Associated hypertension was found in 39% (n=164) of cases compared with 61% (n=256) who were normotensive. The participants' mean (SD) reported duration of diabetes mellitus was 11.5 (7.48) years. The distribution of patients was almost equal among the reported duration categories, with narrow variations. HbA1c was measured by only 78.6% (330) patients, the mean (SD) value of HbA1c was 8.3 (1.7). Among the total, only 22.6% (n=95) patients had normal values of HbA1c (7 or less). The rest of patients had uncontrolled blood glucose level (HbA1c > 7.0).

Table 5.2: Participants' clinical characteristics in relation to type of diabetes, hypertension, diabetes duration and HbA1c

Variable	Categories	% (n)	Mean (SD)
Type of diabetes	Type 1 diabetes	4.8 (20)	
	Type 2 diabetes	95.2 (400)	
Hypertension	No	61.0 (256)	
	Yes	39.0 (164)	
Duration of diabetes/ years	0-5	24.5 (103)	11.5 (7.8)
	6-10	26.7 (112)	
	11-15	23.3 (98)	
	16-60	25.5 (107)	
HbA1c	4.5-7	22.6 (95)	8.3 (1.7)
	7.1-8	17.6 (74)	
	8.1-9.1	19.3 (81)	
	9.2-13.2	19.0 (80)	

5.3.1 Participants' clinical characteristics; determinants of HbA1c:

To examine the effect of the independent variables on the level of blood glucose level among the participants, further analysis was made to find out the relationship between HbA1c (as a dependent variable) and the variables listed in table (5.3). The results of the chi-square test and regression analysis showed that none of the variables listed in the same table was found statistically significant associated with HbA1c. However, there was a trend of increase in the level of HbA1c with increased diabetes duration both in COR and AOR.

Table 5.3: Determinants of HbA1c, (crude and adjusted analysis)

Determinants		Determinants of HbA1c				
		HbA1c value (4.5-7)	HbA1c value (7.1-13.2)	P value	COR (95%CI)	AOR (95%CI)
Gender	Female	29.6% (56)	70.4% (133)	0.71	**1**	**1**
	Male	27.7% (39)	72.3% (102)		1.1 (0.68-1.79)	1.1 (0.70-1.90)
Type diabetes	Type 2	28.9% (90)	71.1% (221)	F 1.00	**1**	**1**
	Type 1	26.3% (5)	73.7% (14)		1.1 (0.39-3.26)	0.9 (0.28-2.72)
Hypertension	No	32.0% (65)	68.0% (138)	0.10	**1**	**1**
	Yes	23.6% (30)	76.4% (97)		1.5 (0.92-2.52)	1.5 (0.88-2.52)
Age group (Years)	30-52	29.3% (24)	70.7% (58)	0.99	**1**	**1**
	53-59	29.1% (25)	70.9% (61)		1.0 (0.52-1.96)	1.0 (0.49-2.03)
	60-65	28.6% (24)	71.4% (60)		1.0 (0.53-2.02)	0.8 (0.40-1.69)
	66-87	28.2% (22)	71.8% (56)		1.1 (0.53-2.09)	0.9 (0.43-1.94)
Diabetes duration (Years)	0-5	34.8% (31)	65.2% (58)	0.39	**1**	**1**
	6-10	30.1% (25)	69.9% (58)		1.2 (0.65-2.35)	1.4 (0.74-2.79)
	11-15	25.0% (18)	75.0% (54)		1.6 (0.81-3.19)	1.8 (0.88-3.68)
	16-60	24.4% (21)	75.6% (65)		1.7 (0.86-3.19)	1.9 (0.95-3.94)
Clinical setting	Outreach	26.7% (73)	73.3% (200)	0.07	**1**	**1**
	Hebron	38.6% (22)	61.4% (35)		0.6 (0.32-1.05)	0.5 (0.30-0.95)

p value significant at ≤0.05, COR: crude OR, AOR: adjusted OR for all variables in the table.
F: fishers exact test (p value not calculated since expected count in one cell less than 5).

5.4 Diabetic eye complications: diabetic retinopathy, cataract and glaucoma

Regarding causes of visual impairment (main diabetic eye complications), participants showed that they developed either a single diabetic complication or multiple complications (combined), as shown in table (5.4). 74.5% of the participants have had some type of diabetic eye complications compared with 25.5% who were found totally free from diabetic eye complications. As single complications, prevalence of diabetic retinopathy, cataract and glaucoma was 42.6% (n=179), 4.8% (n=20) and 2.1% (n=9) respectively. The highest prevalence among multiple causes was for "diabetic retinopathy and cataract" 17.4% (n=73), while the lowest prevalence was for "retinopathy + cataract + glaucoma" 2.4% (n=10). There was one patient (0.2%) who had cataract in which his retinas were invisible for retinal assessment due to opaque eye media. The total number of diabetic complications either single or combined with other causes was 66.6% for retinopathy, cataract 25.5% and glaucoma 9.5%.

Table 5.4: Main diabetic eye complications

Main Diabetic Complications	% (n)
Single Complication	
Diabetic retinopathy	42.6 (179)
Cataract	4.8 (20)
Glaucoma	2.1 (9)
Combined complications	
Diabetic Retinopathy + Cataract	17.4 (73)
Diabetic Retinopathy + Glaucoma	4.3 (18)
Cataract + Glaucoma	0.7 (3)
DR+ Cataract + glaucoma	2.4 (10)
Cataract + no fundus view	0.2 (1)
No complications	25.5 (107)
Total diabetic retinopathy	66.6% (280)
Total cataract	25.5% (107)
Total Glaucoma	9.5% (40)

5.4.1 Determinants of the whole study participants for patients with and without diabetic eye complications:

Table (5.5) depicts the characteristics of the determinants of the whole study participants for patients who developed any type of diabetic eye complications and those who were totally free of diabetic eye complications in regard to age, duration of diabetes and HbA1c. There was no outstanding differences between the two groups regarding their HbA1c; the mean (SD) for patients with eye complications compared with those patients who were free of complications was 8.3 (1.7) versus 8.2 (1.8) respectively. However, patients with diabetic eye complications have had a marked statistically significant (p value= 0.00) higher values compared with patients who were free from eye complications in regard to age and duration of diabetes.

Table 5.5: Mean (SD) of age, duration of diabetes and HbA1c by diabetic eye complications (Diseased vs. non-diseases)

Independent variables		Eye complications	No complications	*p value
Participant Age/ years	No.	313	107	**0.00**
	Mean (SD)	60.0 (9.2)	54.4 (8.4)	
Duration of diabetes/ years	(n)	314	107	**0.00**
	Mean (SD)	13.3 (7.8)	6.2 (4.9)	
HbA1c value	(n)	238	92	0.62
	Mean (SD)	8.3 (1.7)	8.2 (1.8)	

* P value significant at ≤0.05

As table (5.6) shows, logistic regression analysis was used to determine the associations between the determinants listed in the same table and patients who have had diabetic eye complications compared with those who were free from diabetic eye complications (diseased vs. non-diseased). Logistic regression analysis showed that the variables significantly associated with diabetic eye complications, even after adjustment for all variables in the same table (5.6), were hypertension, age, diabetes duration and clinical settings. Subjects who were at increased odds of developing diabetic eye complications were hypertensive patients (AOR=2.3, 95% CI=1.22-4.49) and patients who were older than 59 years (60-65years: AOR=5.0, 95%CI=2.09-12.02) and (66-87years=AOR=3.5, 95%CI=1.45-8.31). Longer duration of diabetes showed an increased odds of developing diabetic eye complications; (6-10 years: AOR=2.4, 95%CI=1.21-4.76), (11-15 years: AOR= 6.4, 95% CI=2.71-14.96) and (16-60 years: AOR= 9.7, 95% CI= 3.48-26.99). For the interval diabetes duration (16-60 years), there was a wide change between COR and AOR values (COR=17.8 to AOR=9.7). Therefore, to examine the effect of the rest of determinants listed in the same table on the value of diabetes duration AOR, each variable was entered separately alongside diabetes duration in the regression model. None of the determinants by itself was shown to be of a marked magnitude on the value of diabetes duration AOR. However, all determinants together appeared to markedly change the value of diabetes duration AOR. For clinical settings, patients who were seen and screened by Hebron clinic were at increased odds of developing diabetic eye complications; (AOR= 2.9, 95%CI= 1.14-7.36). However, logistic regression analysis showed that male gender was not associated with diabetic eye complications (COR=1.5, 95%CI= 0.95-2.36) in the crude analysis, while it was statistically significant after adjustment (AOR=2.0, 95%CI= 1.12-3.81). To estimate the effect of the variables listed in the same table on the value of gender AOR, each variable was entered separately alongside gender variable in the regression model. It was found that both HbA1c and hypertension have changed the value of gender AOR to turn statistically significant associated with diabetes complications. The rest of variables appeared to have no effect on gender as a risk factor to diabetic complications. There was no statistical significant association between the diseased and none diseased patients in relation to HbA1c.

Table 5.6: Determinants of diabetic eye complications, (crude and adjusted analysis)

Determinants		Diabetic eye complication status				
		With complications 74.5% (n=313)	No complications 25.5% (n=107)	P value	COR (95%CI)	AOR (95%CI)
Gender	Female	71.4% (175)	28.6% (70)	0.09	1	1
	Male	78.9% (138)	21.1% (37)		1.5 (0.95-2.36)	**2.0 (1.12-3.81)**
Type of diabetes	Type 2	73.8% (295)	26.3% (105)	F 0.10	1	1
	Type 1	90% (18)	10% (2)		3.2 (0.73-14.04)	4.3 (0.75-25.08)
Hypertension	No	68.4% (175)	31.6% (81)	**0.00**	1	1
	Yes	84.1% (138)	15.9% (26)		**2.5 (1.50-4.03)**	**2.3 (1.22-4.49)**
Age groups Years	30-52	60.4% (64)	39.6% (42)	**0.00**	1	1
	53-59	65.7% (69)	34.3% (36)		1.3 (0.72-2.20)	1.5 (0.69-3.09)
	60-65	84.5% (93)	15.5% (17)		**3.6 (1.88-6.86)**	**5.0 (2.09-12.02)**
	66-87	87.9% (87)	12.1% (12)		**4.8 (2.32-9.76)**	**3.5 (1.45-8.31)**
Diabetes duration (Years)	0-5	48.5% (50)	51.5% (53)	**0.00**	1	1
	6-10	68.8% (77)	31.3% (35)		**2.3 (1.33-4.07)**	**2.4 (1.21-4.76)**
	11-15	86.7% (85)	13.3% (13)		**6.9 (3.44-13.96)**	**6.4 (2.71-14.96)**
	16-60	94.4% (101)	5.6% (6)		**17.8 (7.18-44.32)**	**9.7 (3.48-26.99)**
HbA1c	4.5-7	69.5% (66)	30.5% (29)	0.48	1	1
	7.1-8	67.6% (50)	32.4% (24)		0.9 (0.48-1.76)	0.9 (0.41-2.02)
	8.1-9.1	77.8% (63)	22.2% (18)		1.5 (0.78-3.04)	1.4 (0.63-3.26)
	9.2-13.2	73.8% (59)	26.3% (21)		1.2 (0.64-2.39)	0.8 (0.36-3.26)
Clinical settings	Outreach	70.4% (226)	29.6% (95)	**0.00**	1	1
	Hebron	87.9% (87)	12.1% (12)		**3.0 (1.59-5.83)**	**2.9 (1.14-7.36)**

p value significant at ≤0.05, COR: crude OR, AOR: adjusted OR for all variables in the table.
F: fishers exact test (P value not calculated since expected count in one cell less than 5).

5.4.2 Participants' diabetic eye co-morbidities and diabetic systemic complications:

Other than the main diabetic eye diseases (retinopathy, cataract and glaucoma), some participants were found having other eye co-morbidities, as shown in table (5.7). The prevalence of eye comorbidity among the study sample was 9.1% (38). Out of the total, 3.8% (16) patients were found having retinal detachment and/ or retinal vascular occlusion. Corneal opacities were found in 2.4% (10) of participants. Other co-morbidities like posterior lens capsule opacities, ptyregium, uveitis, retinal diseases and surgical eye complications) were found in 10 (2.4%). Combined co-morbidities (more than one disease listed in the same table) were found in 0.5% (2) of the participants.

Table 5.7: Participants' diabetic eye co-morbidities

Co-morbidity	% (n)	
Retinal detachment and/or retinal vascular occlusion	3.8% (16)	9.1% (38)
Corneal opacity	2.4% (10)	
Others	2.4% (10)	
Combined causes	0.5% (2)	
No comorbidity	91.0% (382)	

According to the development of systematic diabetic complications (neuropathy and nephropathy); there were 0.7% (n=3) patients who have had facial palsy and a similar number 0.7% (n=3) who were found having nephropathy (kidney failure). None of the participants was found with amputated extremities.

5.5 Determinants of diabetic retinopathy

Table (5.8) depicts the mean values difference between patients with retinopathy and those without the disease. Patients who were with retinopathy were a bit older in age mean (SD) = 59.4 (9.18) than those who were free from the disease, mean (SD) = 57.1 (9.41). Similarly, patients with retinopathy have had a remarkable longer duration of diabetes, mean (SD) =13.8 (7.36) compared with patients who were found free of diabetic retinopathy, mean (SD) = 6.9 (6.63). However, there was no outstanding or significant difference between diabetic retinopathy and non diabetic retinopathy subjects in relation to blood glucose control, the two groups have had almost an equal mean blood glucose reading.

Table 5.8: Mean (SD) of age, duration of diabetes and HbA1c by retinopathy status

Independent variables		Retinopathy	No retinopathy	*P value
Participant age, years	No.	280 patients	140 patients	**0.02**
	Mean (SD)	59.4 (9.18)	57.1 (9.41)	
Diabetes duration, years	(n)	280 patients	140 patients	**0.00**
	Mean (SD)	13.8 (7.36)	6.9 (6.63)	
HbA1c value	(n)	210 patients	120 patients	0.98
	Mean (SD)	8.28 (1.69)	8.27 (1.75)	

* p value significant at ≤0.05

As table (5.9) depicts, logistic regression analysis was used to determine the crude and adjusted association between the determinants listed in the same table and patients who have had diabetic retinopathy and those patients who were free from the disease. Logistic regression analysis showed that the variables significantly associated with diabetic retinopathy, even after adjustment for all variables in the same table (5.9), were gender, duration of diabetes, age group (60-65) and clinical settings. For gender, the results showed that retinopathy was more common and

significantly higher among males than females (AOR=1.9, 95% CI=1.12-3.48). To elucidate the association between male gender and retinopathy, further analysis was made to explore the effect of diabetic eye determinants in regard to male/female gender. Results showed that there was no statistical significant difference between males and females for the mean (SD) of age 58.1 (9.37) versus 59.0 (9.26) years, diabetes duration 11.8 (7.34) versus 11.2 (8.16) years and HbA1c 8.1 (1.60) versus 8.4 (1.76). Similar results were found with regard to type of diabetes (p value=0.22), hypertension (p value=0.2) and clinical settings (p value=0.52). Regarding duration of diabetes, retinopathy was found significantly increased with increased duration of diabetes along all diabetes duration categories. Age was also found to be associated with diabetic retinopathy, the result of chi-square test showed a statistical association between age and retinopathy (p value=0.03). However, only patients who fall in the age group category (60-65 years) were at increased odds of developing diabetic retinopathy (AOR=2.2, 95% CI= 1.21-5.97). Diabetic retinopathy was also found to be significantly associated with Hebron clinic setting (AOR=3.9, 95% CI= 1.62-9.41). To elucidate such association, further analysis to diabetic eye determinants in regard to clinical settings was made. Results showed that there were no significant variations between Hebron clinic and outreach settings in regard to age, HbA1c, gender and hypertension. However, duration of diabetes, mean (SD) was statistically significant (p value= 0.003) higher for Hebron clinic patients 13.5 (7.8) years compared with outreach patients 10.8 (7.7) years. In regard to the association of hypertension with diabetic retinopathy, results showed that there was a significant relationship between the two diseases in the crude analysis (COR=1.6, 95% CI= 1.06-2.51). However, hypertension did not sustain its significance after adjustment to the variables in the same table. Further analysis was made to estimate the effect of the variables listed in the same table on the effect of hypertension as a determinant to retinopathy. Each variable was entered separately alongside hypertension in the regression model. It was found that hypertension lost its significance as a diabetic retinopathy risk factor alongside diabetes duration. The rest of variables did not significantly alter the effect of hypertension on diabetic retinopathy. There was no significant relationship (p value=0.91) between diabetic retinopathy and blood glucose level (HbA1c).

Table 5.9: Determinants of diabetic retinopathy, (crude and adjusted analysis)

Diabetic retinopathy determinants		Retinopathy status				
		Retinopathy % (n)	No retinopathy % (n)	P value	COR (95%CI)	AOR (95%CI)
Gender	Female	62.9% (154)	37.1% (91)	**0.05**	1	1
	Male	72.0% (126)	28.0% (49)		**1.5 (1.0-2.31)**	**1.9 (1.12-3.48)**
Diabetes mellitus	Type 2	65.5% (262)	34.5% (138)	F 0.02	1	1
	Type 1	90.0% (18)	10.0% (2)		**4.7 (1.08-20.72)**	**5.9 (1.05-33.17)**
Hypertension	No	62.5% (160)	37.5% (96)	**0.02**	1	1
	yes	73.2% (120)	26.8% (44)		**1.6 (1.06-2.51)**	1.7 (0.92-2.99)
Diabetes duration (Years)	0-5	32.0% (33)	68.0% (70)	**0.00**	1	1
	6-10	60.7% (68)	39.3% (44)		**3.3 (1.87-5.75)**	**3.1 (1.57-6.21)**
	11-15	84.7% (83)	15.3% (15)		**11.7 (5.90-23.36)**	**11.1 (4.88-25.4)**
	16-60	89.7% (96)	10.3% (11)		**18.5 (8.76-39.14)**	**13.1 (5.49-31.7)**
Age group (years)	30-52	57.5% (61)	42.5 % (45)	**0.03**	1	1
	53-59	62.9% (66)	37.1% (39)		1.2 (0.72-2.20)	1.6 (0.74-3.38)
	60-65	75.5% (83)	24.5% (27)		**2.3 (1.27-4.05)**	**2.6 (1.21-5.97)**
	66-87	70.7% (70)	29.3% (29)		1.8 (0.99-3.18)	1.5 (0.66-3.32)
HbA1c	4.5-7	63.2% (60)	36.8% (35)	0.67	1	1
	7.1-8	58.1% (43)	41.9% (31)		0.8 (0.43-1.50)	0.8 (0.36-1.68)
	8.1-9.1	66.7% (54)	33.3% (27)		1.2 (0.63-2.17)	1.0 (0.48-2.19)
	9.2-13.2	66.3% (53)	33.8% (27)		1.2 (0.61-2.14)	0.7 (0.31-1.46)
Clinical settings	Outreach	60.4% (194)	39.6% (127)	**0.00**	1	1
	Hebron	86.9% (86)	13.1% (13)		**4.3 (2.32-8.09)**	**3.9 (1.62-9.41)**

p value significant at ≤0.05, COR: crude OR, AOR: adjusted OR for all variables in the table.
F: fishers exact test (P value not calculated since expected count in one cell less than 5).

5.6 Determinants of cataract

Table (5.10), compares between patients who have had cataract and those who were free from the disease in regard to age, diabetes duration and HBA1c. Results showed a remarkable significant higher mean value for age in patients who were found having cataract, mean (SD) = 64.5 (7.82) compared with patients who were free from cataract, mean (SD) =56.6 (8.93). In regard to duration of diabetes mellitus, there was around 2 years longer difference among those who have had cataract compared with participants who were free of the disease, mean (SD) =13.3 (9.01) versus mean (SD)=10.9 (7.29). As for blood glucose levels, there was no manifest difference between the two groups, table (5.10).

Table 5.10: Mean (SD) of age, duration of diabetes and HbA1c by cataract

Independent variables		cataract	No cataract	*P value
Participant Age/ years	(n)	107	313	**0.00**
	Mean (SD)	64.5 (7.82)	56.6 (8.93)	
Diabetes duration / years	(n)	107	313	**0.00**
	Mean (SD)	13.3 (9.01)	10.9 (7.29)	
HbA1c value	(n)	88	242	0.96
	Mean (SD)	8.28 (1.56)	8.27 (1.76)	

* P value significant at ≤0.05

As table (5.11) depicts, the influence of gender, type of diabetes mellitus, HbA1c, duration of diabetes mellitus and clinical settings as determinants of diabetic eye complications did not show a statistical significant relationship with the development of cataract. However, increased age showed a statistical significant positive increase association with cataract development, patients with older age groups were significantly at increased odds of developing cataract even after adjustment. For hypertension, subjects who were at increased odds of developing cataract were hypertensive patients (COR=1.8, 95% CI= 1.15-2.79), however, hypertension did not retain its significance after adjustment. Further analysis was made to estimate the effect of the variables listed in the same table on the effect of hypertension as a determinant to cataract. Each variable was entered separately alongside hypertension in the regression model. It was found that hypertension lost its significance as cataract risk factor alongside diabetes duration and age. The rest of variables did not significantly alter the effect of hypertension on cataract development. Similarly, for the age group (60-87 years), the value of OR was slightly changed when the rest of the variables in the same table (except HbA1c) were entered in the regression model alongside age determinant. However, when HbA1c was entered in the regression model alongside the rest of variables including age, a marked drop in the age group (60-87 years) OR took place, from (COR= 12.3 95% CI= 5.18-29.08) to (AOR= 8.8, 95% CI= 3.43-22.77).

Table 5.11: Determinants of cataract, (crude and adjusted analysis)

Cataract Determinants		Cataract status				
		cataract % (n)	No cataract % (n)	P value	COR (95%CI)	AOR (95%CI)
Gender	Male	22.3% (39)	77.7% (136)	0.21	1	1
	Female	27.8% (68)	72.2% (177)		1.3 (0.85-2.10)	1.1 (0.60-1.85)
Diabetes mellitus	Type 2	26.3% (105)	73.8% (295)	F 0.12	1	1
	Type 1	10.0% (2)	90.0% (18)		0.3 (0.07-1.37)	0.5 (0.10-2.87)
Hypertension	No	21.1% (54)	78.9% (202)	**0.01**	1	1
	Yes	32.3% (53)	67.7% (111)		**1.8 (1.15-2.79)**	1.3 (0.74-2.29)
Diabetes duration (years)	0-5	19.4% (20)	80.6% (83)	0.10	1	1
	6-10	25.9% (29)	74.1% (83)		1.5 (0.76-2.77)	1.6 (0.73-3.59)
	11-15	22.4% (22)	77.6% (76)		1.2 (0.61-2.37)	0.9 (0.39-2.14)
	16-60	33.6% (36)	66.4% (71)		**2.1 (1.12-3.96)**	1.5 (0.67-3.29)
Age group (years)	30-52	6.7% (7)	93.4% (99)	**0.00**	1	1
	53-59	15.2% (16)	84.4% (89)		**2.5 (1.00-6.47)**	1.5 (0.52-4.08)
	60-65	34.5% (38)	65.5% (72)		**7.5 (3.15-17.67)**	**5.8 (2.28-14.89)**
	66-87	46.5% (46)	53.5% (53)		**12.3 (5.18-29.08)**	**8.8 (3.43-22.77)**
HbA1c	4.5-7	24.2% (23)	75.8% (72)	0.42	1	1
	7.1-8	27.0% (20)	73.3% (54)		1.2 (0.58-2.32)	1.2 (0.55-2.59)
	8.1-9.1	33.3% (27)	66.7% (54)		1.6 (0.81-3.02)	1.6 (0.74-3.27)
	9.2-13.2	22.5% (18)	77.5% (62)		0.9 (0.45-1.84)	0.9 (0.39-1.94)
Clinical setting	Outreach	25.9% (83)	74.1% (238)	0.75	1	1
	Hebron	24.2% (24)	75.8% (75)		0.9 (0.54-1.54)	1.2 (0.57-2.43)

p value significant at ≤0.05, COR: crude OR, AOR: adjusted OR for all variables in the table.
F: fishers exact test (P value not calculated since expected count in one cell less than 5)

5.7 Determinants of glaucoma

Table (5.12), compares between patients who have had glaucoma and those who were free from the disease in regard to age, diabetes duration and HbA1c. There was no significant difference between mean (SD) for age and duration of diabetes in regard to glaucoma. However, there was a manifest difference between patients who had glaucoma and those who were free from the disease in regard to HbA1c. Patients with glaucoma have had a statistical significant (p value= 0.00) higher mean (SD) of HbA1c, 9.08 (1.94) compared with glaucoma free patients, 8.19 (1.66). Table 5.12: Mean (SD) of age, duration of diabetes and HbA1c by glaucoma

Independent variables		Glaucoma	No glaucoma	*P value
Participant Age/ years	(n)	40	380	0.11
	Mean (SD)	60.9 (7.37)	58.4 (9.47)	
Diabetes duration / years	(n)	40	380	**0.10**
	Mean (SD)	13.4 (10.03)	11.3 (7.54)	
HbA1c value	(n)	29	301	**0.00**
	Mean (SD)	9.08 (1.94)	8.19 (1.66)	

* P value significant at ≤0.05

As table (5.13) shows, the influence of the determinants listed in the same table did not show a statistical significant association with glaucoma development except for the HbA1c category (9.2-13.2). Logistic regression analysis showed that only those participants who had the highest HbA1c level (9.2-13.2) were statistically significant associated with glaucoma development even after adjustment to the variables in the same table (AOR=3.1, 95%CI=1.15-8.62), table (5.13).

Table 5.13: Determinants of "glaucoma status", (crude and adjusted analysis)

Glaucoma Determinant		Glaucoma Status				
		Glaucoma % (n)	No Glaucoma % (n)	P value	COR (95%CI)	AOR (95%CI)
Gender	Female	9.0% (22)	91.0% (223)	0.65	**1**	**1**
	Male	10.3% (18)	89.7% (157)		1.2 (0.60-2.24)	1.1 (0.49-2.53)
Diabetes mellitus	Type 2	9.8% (39)	90.3% (361)	F 0.48	**1**	**1**
	Type 1	5.0% (1)	95.0% (19)		0.5 (0.06-3.74)	0.4 (0.40-3.49)
Hypertension	No	7.8% (20)	92.2% (236)	0.14	1	1
	yes	12.2% (20)	87.8% (144)		1.6 (0.85-3.15)	2.1 (0.92-4.92)
Diabetes duration (Years)	0-5	8.7% (9)	91.3% (94)	0.85	**1**	**1**
	6-10	8.0% (9)	92.0% (103)		0.9 (0.35-2.39)	0.4 (0.11-1.51)
	11-15	10.2% (10)	89.8% (88)		1.2 (0.46-3.06)	0.9 (0.28-2.70)
	16-60	11.2% (12)	88.8% (95)		1.3 (0.53-3.28)	0.7 (0.20-2.11)
Age group (Years)	30-52	6.6% (7)	93.4% (99)	0.19	**1**	**1**
	53-59	7.6% (8)	92.4% (97)		1.2 (0.41-3.34)	0.7 (0.18-2.38)
	60-65	14.5% (16)	85.5% (94)		2.4 (0.95-6.11)	2.1 (0.69-6.39)
	66-87	9.1% (9)	90.9% (90)		1.4 (0.51-3.95)	0.5 (0.13-2.26)
HbA1c	4.5-7	6.3% (6)	93.7% (89)	**0.02**	**1**	1
	7.1-8	6.8% (5)	93.2% (69)		1.1 (0.31-3.67)	1.2 (0.32-4.14)
	8.1-9.1	4.9% (4)	95.1% (77)		0.8 (0.21-2.83)	0.7 (0.19-2.80)
	9.2-13.2	17.5% (14)	82.5% (66)		**3.1 (1.15-8.62)**	**3.2 (1.08-9.56)**
Clinical settings	Outreach	9.7% (31)	90.3% (290)	0.86	**1**	**1**
	Hebron	9.1% (9)	90.9% (90)		0.9 (0.43-2.04)	1.7 (0.58-5.42)

p value significant at ≤0.05, COR: crude OR, AOR: adjusted OR for all variables in the table.
F: fishers exact test (P value not calculated since expected count in one cell less than 5).

5.8 Determinants of the participants' visual acuity status / Overall outcome

Figure (5.1) summarizes the participants' best corrected visual acuity status based on the WHO definition. Prevalence of "low vision" and "blindness" was 30.2% (127) and 5.5% (23) respectively, giving an overall visual impairment (VI) prevalence of 35.7%.

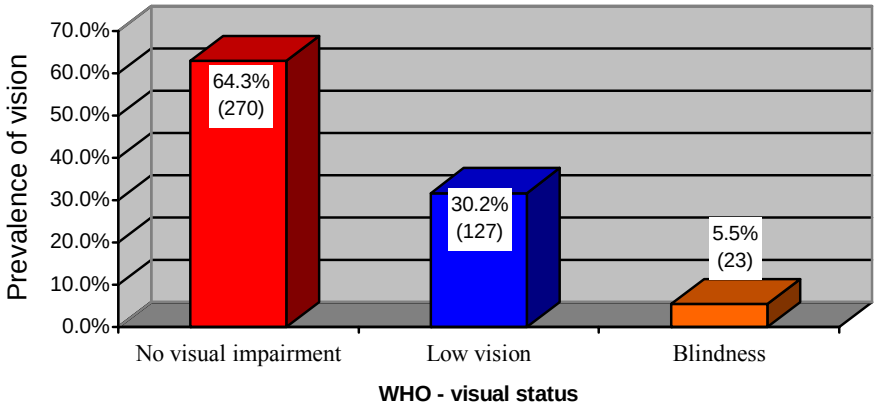

Figure 5.1: participants' visual status

To better elucidate the effect of diabetic determinants on the ocular status, we further examined the effect of diabetic determinants on visual status. Table (5.14) compares the value differences for visually impaired and normal vision participants regarding age, duration of diabetes and HbA1c. For age, the mean value of visually impaired subjects was found around 6 years significantly higher than patients who had not visual impairment, mean (SD)= 62.3, (8.28) versus mean (SD)= 56.6, (9.22) years respectively. Similar results were found regarding duration of diabetes, (SD)= 14.5, (8.27) versus mean (SD)= 9.8 (7.04) years respectively. There was no noticeable difference in HbA1c between the two groups, table (5.14).

Table 5.14: Mean (SD) age, duration of diabetes and HbA1c by WHO visual impairment

Independent variables		Visual impairment	No Visual impairment	*P value
Participant Age/ years	(n)	150	270	**0.00**
	Mean (SD)	62.3 (8.28)	56.6 (9.22)	
Duration diabetes/ years	(n)	150	270	**0.00**
	Mean (SD)	14.5 (8.27)	9.8 (7.04)	
HbA1c value/ years	(n)	111	219	0.20
	Mean (SD)	8.4 (1.61)	8.2 (1.75)	

* P value significant at ≤0.05

Table (5.15), displays the prevalence of visual status (WHO definition) among the study participants according to the study determinants strata. Logistic regression analysis showed that hypertension, age, duration of diabetes and clinical settings were significantly associated with visual impairment even after adjustment to the variables in the same table (5.15). Hypertensive patients were significantly at increased odds of having visual impairment (AOR=1.8, 95% CI= 1.03-3.07). Subjects who were 60 years and above were found statistically significant at increased risk of developing visual impairment, (60-65years: AOR=4.2, 95%CI=1.79-9.62) and (66-87 years: AOR=3.51, 95%CI= 1.47-8.35). Regarding duration of diabetes mellitus, patients who were above 10 years duration of having diabetes mellitus were found statistically significant at increased odds of having visual impairment; (11-15years: AOR=2.7, 95%CI= 1.05-6.90) and (16-60 years: AOR=3.9, 95%CI=1.46-10.99). Similarly, Hebron clinic patients showed a statistical significant positive increase risk of developing visual impairment compared with outreach patients (AOR=3.9, 95%CI=1.76-8.82). To elucidate such association in regard to clinical settings, further analysis to diabetic eye determinants in regard to clinical settings was made. Results showed that there were no significant variations between Hebron clinic and outreach settings in regard to age, HbA1c, gender and hypertension. However, duration of diabetes, mean (SD) was statistically significant (p value= 0.003) higher for Hebron clinic patients 13.5 (7.8) years compared with outreach patients 10.8 (7.7) years. Gender and type of diabetes were not found to be association with visual impairment. For HbA1c category 8.1-9.1, it showed a statistically significant relationship with visual impairment in the crude analysis (COR=1.9, 95%CI= 1.02-3.64). However, it lost its significance once both variables (hypertension and duration of diabetes) were entered in the regression model alongside HbA1c (AOR=1.8, 95%CI= 0.90-3.85), table (5.15).

Table 5.15: Determinants of "visual status", (crude and adjusted analysis)

Determinants		WHO visual status				
		Visual impairment	No visual impairment	P value	COR (95%CI)	AOR (95%CI)
Gender	Male	34.9 % (61)	65.1% (114)	0.75	**1**	**1**
	Female	36.3 % (89)	63.7% (156)		1.1 (0.71-1.59)	0.9 (0.53-1.56)
Type diabetes	Type 2	36.3% (145)	63.7% (255)	0.31	**1**	**1**
	Type 1	25.0 % (5)	75.5% (15)		0.6 (0.21-1.65)	0.7 (0.18-2.24)
Hypertension	No	29.7% (76)	70.3% (180)	**0.00**	**1**	**1**
	Yes	45.1% (74)	54.9% (90)		**1.9 (1.29-2.92)**	**1.8 (1.06-3.09)**
Age group (Years)	30-52	18.9% (20)	81.1% (86)	**0.00**	**1**	**1**
	53-59	25.7% (27)	74.3% (78)		1.5 (0.77-2.86)	1.5 (0.63-3.53)
	60-65	49.1% (54)	50.9% (56)		**4.1 (2.25-7.65)**	**4.4 (1.95-10.05)**
	66-87	49.5% (49)	50.5% (50)		**4.2 (2.25-7.88)**	**3.5 (1.53-8.25)**
Diabetes duration (Years)	0-5	19 (18.4%)	81.6% (84)	**0.00**	**1**	**1**
	6-10	29.5% (33)	79 (70.5%)		1.8 (0.97-3.51)	1.7 (0.78-3.92)
	11-15	37.8% (37)	62.2% (61)		**2.7 (1.41-5.10)**	**2.6 (1.15-5.83)**
	16-60	57.0% (61)	43.0% (46)		**5.9 (3.13-10.99)**	**4.7 (2.13-10.26)**
HbA1c	4.5-7	26.3% (25)	73.7% (70)	0.22	**1**	**1**
	7.1-8	32.4% (24)	67.6% (50)		1.3 (069-2.62)	1.6 (0.80-3.57)
	8.1-9.1	40.7% (33)	59.3% (48)		**1.9 (1.02-3.64)**	1.8 (0.90-3.85)
	9.2-13.2	36.3% (29)	63.8% (51)		1.6 (0.84-0.04)	1.3 (0.66-2.90)
Clinical setting	Outreach	104 (32.4%)	217 (67.6%)	**0.01**	**1**	**1**
	Hebron	46 (46.5%)	53 (53.5%)		**1.8 (1.14-2.86)**	**3.9 (1.76-8.82)**

p value significant at ≤0.05, COR: crude OR, AOR: adjusted OR for all variables in the table.
F: fishers exact test (P value not calculated since expected count in one cell less than 5).

Table (5.16) illustrates the exclusive diabetic eye complications associated with WHO visual impairment among our study participants. For exclusive single complications, diabetic retinopathy, cataract and glaucoma accounted for 31.1% (n=47) patient, 6.0% (n=9) patient and 0.7% (n=1) patient of WHO visual impairment respectively. For multiple determinants, retinopathy and cataract (combined) accounted for the largest share of visual impairment 36.7% (n=55) patient. Other than (combined diabetic retinopathy and cataract), multiple causes of the main diabetic eye complications were associated with 10.7% (n=16) visual impairment. For those patients who were found having both (one of the main diabetic eye complication/s) and others (eye co-morbidities), visual impairment was present in 14.7% (n=22) patient, table (5.16).

Table 5.16: Exclusive diabetic eye complications associated with visual impairment

Diabetic eye complication	**Visual impairment 35.7% (150 patients)**
Diabetic retinopathy	31.3% (47)
Cataract	6.0% (9)
Glaucoma	0.7% (1)
Diabetic retinopathy + Cataract	36.7% (55)
Multiple causes of main diabetic eye complications	10.7% (16)
Main complication/s + co-morbidity	14.7% (22)
Total	100% (150)

5.9 Chapter summary

The chapter included the results of the study frequencies and percentages of the independent and dependent variables. The relationship between the main diabetic eye complications (retinopathy, cataract, glaucoma) and their determinants was examined by chi-square test, and further by the binary logistic regression, both unadjusted and adjusted odds ratios. The chapter ended up with examining the relationship between the WHO visual impairment status and the diabetic eye risk factors (determinants) through calculating both chi-square test and odds ratios. Analysis went further to find out, exclusively the association between diabetic eye complications and WHO visual impairment among the study sample.

Chapter Six. Discussion, Conclusions and Recommendations

6.1 Introduction

In the present study, we estimated the prevalence of the main diabetic eye complications (retinopathy, cataract, glaucoma) and their impact on visual acuity among a diabetic sample that was screened and treated by St. John Eye Hospital. It further examined the effects of diabetic eye determinants namely, gender, type of diabetes, hypertension, duration of diabetes, age, blood glucose level and clinical settings on the development of diabetic eye complications and related visual impairment. Discussion of the study results is presented in this chapter along with conclusions and recommendations.

6.2 Prevalence of diabetic eye complications and their association with diabetic eye determinants

Diabetic retinopathy, cataract and glaucoma were present in 66.6%, 25.5% and 9.5% of the study participants respectively. Out of the total study participants, visual impairment was present in 35.7%. Age, was found to be significantly associated with retinopathy, cataract and visual impairment, but not with glaucoma. In adjusted analysis, only patients who were between (60-65 years) were found significantly at increased odds of developing retinopathy. While, those patients who were ≥ 60 years showed a significant increased odds of developing both cataract and visual impairment.

Duration of diabetes was found to be significantly associated with Diabetic retinopathy and visual impairment, but was not related to glaucoma and cataract. In multivariate analysis, duration of diabetes sustained significance as a risk factor to diabetic retinopathy along all diabetes duration categories. However, only those patients who had diabetes duration ≥11 years remained significantly at increased odds of developing visual impairment.

Adjusted analysis showed that hypertension was found to be significantly associated visual impairment, but was not related to diabetic retinopathy, cataract and glaucoma. For HbA1c, adjusted analysis revealed that only patients with the highest HbA1c readings (9.2-13.2) remained significantly at increased odds of developing glaucoma. HbA1c was not related to diabetic retinopathy, cataract and visual impairment. Adjusted analysis showed that male gender was found to be an independent significant risk factor for diabetic retinopathy, but not for cataract, glaucoma and visual impairment. Hebron clinic setting was found to be an independent determinant for diabetic retinopathy and visual impairment, no association was found with cataract and glaucoma. Diabetic retinopathy, cataract and glaucoma contributed to (31.1%), (6.0%) and (0.7%) of visual impairment respectively. Diabetic retinopathy and cataract as a combined cause, contributed to (36.7%) of visual impairment.

6.3 Effect of diabetic eye risk factors on diabetic eye complications

In the following paragraph, the author aimed at comparing the main study results with findings from previous related studies regarding the effect of the main diabetic eye risk factors on the development of diabetic eye complications and further on visual status.

6.3.1 Effect of diabetic eye risk factors on diabetic retinopathy:

In our study, prevalence of diabetic retinopathy was found to be 66.6%. It was higher than it was found in Jordan (64.1%), Oman (42.4%), Al-Ain-United Arab Emirates (19%) and Istanbul (42.8%), (Till et al, 2005), (Haddad and Saad, 1998), (Maskari and Elsadig, 2007) and (Karadeniz and Yilmaz, 2007) respectively. The narrow difference in diabetic retinopathy prevalence between the present study and the Jordanian was most probably due to the fact that both settings share a wide spectrum of geographical, economical and ethnic characteristics. On the other hand, unlike our study participants who were attendants of an eye clinic, the participants of the Omani, United Arab Emirates and Istanbul patients were either diabetic clinic attendants or house hold participants. This might bias our results since our study participants might presented for examination due to certain visual defects. However, it could be due to the severity of diabetic eye complications or as a result of other different risk factors among our study sample. In line with this, diabetic retinopathy may be influenced by several factors like accessibility of care, efficacy of coordination among different health professionals, socioeconomic status, life style and social support (Shazly et al, 2000).

In the present study, diabetic retinopathy was more common among males than females even after adjustment to the variables listed in table (5.9). Similarly, in aforementioned Al-Ain study, retinopathy was more common among males (24.2%) than females (13.9%) (Maskari and Elsadig, 2007). In the contrary, no association between gender and diabetic retinopathy was found in both Oman (Haddad and Saad, 1998) and Victoria –Australia, (McCarty et al, 2000). To elucidate the association between male gender and retinopathy in the present study, further analysis was made to explore the effect of diabetic eye determinants in regard to male/female gender.

As shown in paragraph (5.5), results showed that there was no statistical significant difference between males and females for all diabetic eye risk factors that were investigated in the present study. In regard with this, Shazly et al, reported that several factors relating to personal characteristics, clinical variables and delivery of care have an important role in the development and/or progression of diabetic retinopathy, (Shazly et al, 2000). Such diabetic retinopathy risk factors could have raised the difference in the prevalence of diabetic retinopathy among both sexes in this study. In line with this, further investigations which aim at investigating retinopathy among Palestinian male gender would minimizes the burden of the disease among such risky group. In our study, diabetic retinopathy was significantly higher among type 1 diabetes patients compared with type 2 diabetes patients.

After adjustment to the risk factors listed in table (5.9), it was marginally significant but showed a five folds increased risk. However, only 4.8% of our patients had type 1 diabetes. Similarly, the findings of the aforementioned Al-Ain study (Maskari and Elsadig, 2007) and a case control study in Egypt (Shazly et al, 2000) found that type 1 diabetes was a significant contributing risk factor for diabetic retinopathy compared with type 2 diabetes. Our findings were consistent with the literature. Type 1 diabetes is usually associated with longer duration of exposure to diabetic eye risk factors than type 2 diabetes. This is because type 1 appears early in life. Epidemiological data have shown that the natural history of retinopathy is similar in both types. However, the prevalence is higher and the severity greater in people with type 1 because retinal changes usually do not occur without long-standing hyperglycemia, the case of type 1 diabetes (Shazly et al, 2000) In respect with this, close attention and follow up for patients with type 1 diabetes should be initiated and highlighted in diabetes management approaches.

In the present study, diabetic retinopathy was found significantly associated with duration of diabetes and age. Our results were consistent with the findings of aforementioned Al-Ain and Omani studies where diabetic retinopathy was found statistically significant associated with increasing age and diabetes duration (Maskari and Elsadig, 2007 and Haddad and Saad, 1998). In line with this, the authors reported that duration of diabetes is known to reflect the period of exposure to the total blood glycemic levels and other diabetic risk over time. Of course, longer duration periods are associated with older age subjects. After 20 years duration, nearly all type 1 diabetes patients and approximately two thirds of type 2 diabetes end up with diabetic retinopathy. Micro and macro vascular diabetic complications including retinal changes are most likely caused by hyperglycemia and associated diabetic risk factors overtime (Maskari and Elsadig, 2007).

In the present study, it was found that among subjects with duration of diabetes 0-5 years, have had a markedly high prevalence of diabetic retinopathy (32.0%). Such result indicates an early onset of retinopathy comparable with the short period of diabetes duration (0-5 years). While such early diabetic retinopathy development could be due to the severity of diabetic eye risk factors; a delay in diabetes clinical diagnosis could have occurred. In line with this, Haddad and Saad in their aforementioned study highlighted that estimating time duration of diabetes could be compromised due to delay in diabetes clinical diagnosis. A gap between the onset of diabetes and clinical diagnosis could exist in patients with type 2 diabetes. This leads to a bias in estimating the reported time duration of diabetes (Haddad and Saad, 1998). Similar to our findings, in India, Agrawal et al, found that increased prevalence of diabetic retinopathy was found associated with increased duration of diabetes among type 2 diabetes. The authors added that estimating the reported time duration of diabetes could give different estimations of the prevalence of retinopathy as clinical diagnosis of type 2 diabetes could be delayed (Agrawal et al, 2003). In respect with this, proper planning for better identification of diabetic cases in the Palestinian community should be initiated. This will shorten the gap between the onset of the disease and its clinical diagnosis. Arguably, if the early diabetic retinopathy development among our study participants was due to the severity of risk factors, a depth review to diabetic management programs in the Palestinian community is required.

In the present study, unlike the findings elsewhere, HbA1c was not related to diabetic retinopathy. However, the best evidence regarding HbA1c comes from the systemic review of all English language articles (1966 through May 2007) by Mohamed et al, 2007. The review included 44 articles (randomized controlled trials including DCCT, UKPDS and meta-analyses) that evaluated management of diabetic ocular complications. It was found that HbA1c at normal values reduces both the development and progression of diabetic retinopathy. Over 6.5 years of follow-up, the diabetes control and complications trial (DCCT-1983 and 1993, randomized 1441 patients with type 1 diabetes) found that intensive treatment (median HbA1c, 7.2%) reduced the incidence of diabetic retinopathy by 76% (95% CI, 62%-85%) and progression of diabetic retinopathy by 54% (95% CI, 39%-66%), as compared with conventional treatment (median HbA1c, 9.1%). For each 10% decrease in HbA_{1c} level (eg, 9% to 8%) reduces the risk of diabetic retinopathy by 39%. Such findings were also supported by the Prospective Diabetes Study-UK (UKPDS-the largest and longest from 1977-1991 with randomized 3867 persons newly diagnosed type 2 diabetes) where intensive therapy (median HbA1c=7.0%) was found to reduce diabetic retinopathy by 25% (95% CI, 7%-40%) compared with the conventional therapy group (median HbA1c=7.9%). Results showed that every percentage point decrease in HbA1c (e.g., 9 to 8%) there was a 35% reduction in the risk of microvascular complications. However, there was no threshold for HbA1c level as a cut point to complication development (Mohamed et al, 2007, Diabetes Control and Complications Trial Research Group, 1995 and Genuth et al, 2002). In line with this, the degree of blood glucose level over the whole diabetes duration time (rather than merely a period of three months that is reflected by HbA1c values) is the key issue regarding the association of blood glucose level and progression of diabetic retinopathy. Such fact might explain the absence of association between diabetic retinopathy and HbA1c in the present study. It was possible that our study patients had experienced high blood glucose levels for a long time prior to the study data collection phase. A certain degree of improvement to their blood glucose level took place in different levels among different subjects once they had been under medical observation.

Moreover, the majority of our study participants (71.2%) showed uncontrolled blood glucose level (HbA1c > 7.0). This further supports the probability that our study subjects have had above the normal blood glucose levels for a long time period prior to the study data collection phase. Comparably, the aforementioned previous Omani study found that the degree of glycemic control failed to retain its significance (after adjustment to a number of diabetic risk factors) as an independent risk factor for retinopathy. Failure to show this association may be because the fasting blood glucose level did not reflect the control of diabetes over the whole time duration of diabetes (Haddad and Saad, 1998). On the other hand, it is worth mentioning that diabetic retinopathy is of variable stages according to the progression and severity of the disease, ranging from early signs of the disease to severe damage of the retinal structure (proliferative diabetic retinopathy) and vision-threatening diabetic maculopathy. Arguably, the present study failed to demonstrate an association between the level of HbA1c and diabetic retinopathy because it did not take into consideration the specific stage of diabetic retinopathy so as to be examined with the level of HbA1c or at least with the need of laser photocoagulation. On this basis, the explanation to the absence of association between retinopathy and blood glucose level in our study

could be made. Klein R, reported that the results of the largest studies of UKPDS (Prospective Diabetes Study-UK) and the DCCT (Diabetes Control and Complications

Trial-America) have provided further support for the American Diabetes Association's guidelines of a target HbA1c goal of 7.0%. However, data from the WESDR (Wisconsin Epidemiological Study of Diabetic Retinopathy-type 1-America) and the National Health and Nutrition Examination Survey III suggest that few persons with diabetes reach this level of glycemic control (Klein, 2002). Good metabolic control is associated with less diabetic care expenditure as it is associated with less diabetic complications (Zakwani et al, 2006). In line with this, improving blood glucose level among Palestinian diabetics would in turn hinder or at least delay diabetic retinopathy development.

Our study showed a statistically significant association between diabetic retinopathy and hypertension. However, the association failed to sustain its significance when treated in the multivariate regression model. We compared our findings with results from different epidemiological studies. Similar to our findings, Klein BE and Klein R did not find an association between hypertension and diabetic retinopathy in patients having type 2 diabetes (Klein BE and Klein R, 2006). In the contrary, the Omani study, reported that hypertension was found to be statistically significant associated with diabetic retinopathy (Haddad and Saad, 1998). Similarly, Tapp R et al, found that improved monitoring and control of hypertension in patients with diabetes could reduce the number of people developing diabetic retinopathy since hypertension has frequently been shown to be a risk factor for the development of diabetic retinopathy **(**Tapp R et al, 2003)**.** Increased blood pressure, through an effect on blood flow, has been hypothesized to damage the retinal capillary endothelial cells. Hence, blood pressure control reduces the risk of diabetic retinopathy (Negi and Vernon, 2003).

In our study, absence of significant association between hypertension and diabetic retinopathy in the multivariate regression model could have been undermined by other risk factors. However, it is worth highlighting that in the present study it was not possible to differentiate between neither the level of hypertension control (systolic or diastolic blood pressure) nor the type of antihypertensive medications among patients with and without retinopathy. All of which could have altered the association between hypertension and diabetic retinopathy. In line with this, the UKPDS, showed that after 9 years of follow-up (randomized 1048 patients with hypertension, tight blood pressure control <150/<85 mm Hg and conventional control <180/<105 mm Hg) found that patients having tight control had a 34% reduction (99% CI, 11%-50%) in retinopathy progression compared with those having conventional control. It was found that each 10-mm Hg decrease in systolic blood pressure reduces the risk of microvascular complications by 13%, independent of glycemic control. The UKPDS concluded that tight blood pressure control (mean 144/82 mm Hg) achieved significant reductions in diabetic retinopathy occurrence, blood pressure should be kept below 130/85mmhg. Moreover, the study also showed that there was a continuous relationship between systolic blood pressure and diabetic retinopathy. Nonetheless, there was no evidence of a threshold for retinopathy above a systolic pressure of 130 mmHg (Matthews et al, 2004, Genuth et al, 2002 and Mohamed et al, 2007). The inconsistency of lowering blood pressure effect on reducing diabetic retinopathy could be affected by the type of antihypertensive agents. The systemic review of 44 articles that where reviewed by

Mohamed et al, 2007 revealed that ACE inhibitors (antihypertensive agents) have an additional benefit on diabetic retinopathy progression independent of blood pressure lowering. However, data from the UKPDS did not find ACE inhibitors to be superior to other blood pressure medications (Mohamed et al, 2007), (Donnelly et al, 2000). Unlike the findings elsewhere, associated hypertension in our study was most probably under diagnosed (39.0%). However, this was presumably due to that our study did not physically examine patients for the presence of hypertension, rather it was considered reportedly. Comparably, in Italy, Mancia found that type 2 diabetes mellitus and hypertension are comorbid clinical conditions that synergize to create vascular changes. The large majority of patients with newly diagnosed Type 2 diabetes are hypertensive (Mancia, 2007). Additionally, Donnelly et al, reported that hypertension affects at least 50% of patients with diabetes where Teitelbaum et al, found that 74.4% of their diabetic sample reported to have hypertension, (Donnelly et al, 2000) (Teitelbaum et al, 2005). While this probably could explain the absence of independent association between hypertension and diabetic retinopathy in the present study, it is of great importance to high light the probability of missed diagnosed hypertension cases among diabetic Palestinians. In line with this, screening for hypertension among Palestinian diabetics for better detection of the disease should be reviewed by the concerned health care planners.

Our study results showed a statistically significant association between diabetic retinopathy and clinical settings. Hebron clinic patients were more prone to diabetic retinopathy than outreach patients. This result could be possible due to the longer diabetes duration among Hebron clinic patients, mean (SD) =13.5 (7.82) years compared with outreach patients, mean (SD) =10.8 (7.73) years. Additionally, unlike outreach clinic which heavily provides free of charge diabetic eye screening services, Hebron clinic provides more secondary care and less free of charge services. Arguably, Hebron clinic patients sought eye care a bit late than outreach patients. However, a wide range of risk factors could have raised the difference of retinopathy regarding clinical settings. In line with this, Agrawal et al, reported that the reasons for differences of diabetic retinopathy prevalence among different people in various locations are not clear. It could be due to the influence of socio-economical, environmental and cultural factors (Agrawal et al, 2003). Consequently, the importance of well-organized diabetic eye screening programs should be initiated on the national level so as to overcome all possible diabetic eye risk factors and ensure early detection and intervention. Furthermore, raising health awareness among diabetics regarding early detection is important. Routine check up and regular eye examination at health care facilities should not be considered only when only getting eye problems or drop in visual acuity. In the contrary, eye care settings should be viewed from a primary health care perspective rather than merely curative settings for secondary and tertiary eye care.

6.3.2 Effect of diabetic eye risk factors on cataract development:

As mentioned earlier in chapter three (3.5.4), cataract formation is of many types and classifications. It has multiple risk factors ranging from biological to socio-economical and environmental factors (Janghorbani et al, 2000). Hence, to examine the association between cataracts formation with different cataract risk factors alongside diabetic eye risk factors is

very limited in a cross-sectional study. Yet, closely related findings from the literature have been explored in the present study.

In the present study, one quarter of the study subjects (25.5%) was found to have cataract. It was less than the findings of the aforementioned study in Jordan (37.8%), (Till et al, 2005) but higher than the findings that were reported in Sweden (19%), (Olafsdottir et al, 2007) and Brazil (19.8%), (Esteves et al, 2008). Chuang et al, estimated the prevalence of cataract among diabetics using data that was collected by 194 centers from eight Asian countries (East Asia) between 2001-2002. Their results showed a prevalence of cataract of 6% among patients who were diagnosed with diabetes before 30 years old and 23% among patients who were diagnosed with diabetes at 30 years old and above (Chuang et al, 2006). The difference in cataract prevalence among the present study participants compared with others could be possible due to the sampling variations. While our sample subjects were an eye clinic attendants, the above mentioned studies subjects were a diabetic clinic or house hold subjects. Moreover, epidemiological studies reported variations in cataract prevalence among different groups. There is a 5-10 fold global variation in the prevalence of blinding cataract (Johnson et al, 1998).

In the present study, age was found to be statistically significantly associated with cataract. In the multivariate analysis, patients who were $\geq$ 60 years remained significantly at increased odds of cataract formation. Such findings were consistent with many epidemiological studies elsewhere. Klein BE and Klein R found that nuclear cataract, cortical cataract and sub-capsular cataract were found to be associated with increasing age among diabetics (Klein BE and Klein R, 2006). Similarly, Janghorbani et al., reported that age was found to be a significant independent predictor of cataract among a diabetic sample (Janghorbani et al, 2000). Tung T et al, found that all types of cataract were found strongly associated with age among type 2 diabetics (Tung et al, 2005). Similarly, Esteves et al, found that age was independently associated cataract formation among type 1 diabetic patients (Esteves et al, 2008). In line with this, Johnson et al, reported that several epidemiological studies that were undertaken in both developed and developing countries found that age is the strongest risk factor for cataract. The risk of cataract associated with diabetes is age dependent. With increased age, the changes of the eye lens protein, lead to opacity and eventually to cataract formation (Johnson et al, 1998).

In our study, as shown in tables (5.10) and (5.11), cataract patients were markedly older in age than non-cataract patients. It is worth mentioning that all types of cataract were found by a large number of epidemiological studies that focused on either diabetic or general populations to be associated with age. Similarly, age was also found to be associated with high prevalence of surgical cataract among different populations (Tsai et al, 2007). In line with this, our study findings seem to have a consistency with the findings elsewhere where age exerts marked contribution to cataract formation.

In the present study, hypertension was found to be statistically significantly associated with cataract development. After adjustment to diabetic eye risk factors listed in table (5.11), hypertension did not remain significant. Comparably, Janghorbani et al, found that hypertension was not related to cataract (Janghorbani et al, 2000). However, hypertension was found to be a risk factor for cataract among types 1 and 2 patients (Ughade et al, 1998

and Esteves et al, 2008). On the other hand, Tung T et al found that cataract was associated with lower diastolic blood pressure (Tung et al, 2005). In respect with this, Tsai et al, reported that the plausible biological mechanisms that link hypertension to cataract remain uncertain. The association of blood pressure with any type of cataract has been reported by different research studies. Some studies have suggested the role of antihypertensive medications as possible risk factors for cataract. Yet, further epidemiological and etiological investigations are needed to clarify the pathophysiological mechanisms between blood pressure and cataract among diabetic population (Tsai et al, 2007). In line with this, it was not possible for our study to have neither the value readings of blood pressure (systolic or diastolic blood pressure) nor the use of antihypertensive medications so as to examine the association between cataract formations with blood pressure. Moreover, our study considered the reported hypertension rather than physical examination for hypertension which further would compromise and under estimate hypertension prevalence in our study. All of which would have compromised the association between the two diseases.

In our study, HbA1c and duration of diabetes were not associated with cataract. Unlike our findings, Janghorbani et al, found that HbA1c and duration of diabetes were statistically significantly associated with cataract formation (Janghorbani et al, 2000). Additionally, Kim S and Kim S.J reported that duration of diabetes was found to be the strongest risk associated with cataract. However, similar to our results they found that blood glucose level was not related to cataract formation. They reported that HbA1c that was used as an indicator to blood glucose control did not reflect blood glucose level for the whole diabetic duration. Duration of diabetes reflects the effect of hyperglycemia accumulation on the eye lens over the whole time period of diabetes. It disturbs the eye lens transparency and induces cataract. They further elaborated that it is the duration of diabetes which contributes to cataract formation over time because it reflects the true average value of blood glucose during the patients' diabetic period rather than the level of HbA1c which usually reflects blood glucose level for a short period of time. Hence, a direct relationship between HbA1c and cataract was not found in most prevalent studies (Kim S and Kim S.J, 2006). Similarly, HbA1c reading value in the present study did not reflect the participants' blood sugar level for the whole period of their diabetic duration. The absence of association between cataract and duration of diabetes in our study could have been masked by many other important risk factors. As shown in paragraph (3.4.2.3 cataract risk factors), smoking, diet, socioeconomic status, myopia, genetic factors, use of insulin, body mass index, steroid therapy and ultraviolent light were all found to be risk factors for cataract formation. Moreover, the present study did not classify cataract into its different types, whereas it is well known that diabetes is associated with cortical and sub-capsular cataracts more than it is with the rest of other cataract types (Rowe N et al, 2000). Additionally, large epidemiological studies failed to demonstrate an association between diabetes duration and different cataract formation. On the other hand, as mentioned earlier, the type of diabetic treatment was found to have an effect on different cataract types, the case of oral hypoglycemic therapy that found to be associated with sub-capsular cataract (Rowe N et al, 2000). Arguably, lack of classification of both cataract and hypoglycemic therapy into their different types has weakened the association between duration of diabetes and cataract. Finally, among the present study participants, there was no marked difference between

cataract patients and non-cataract patients regarding duration of diabetes and HbA1c, tables (5.10 and 5.11). Presumably, this was one of the reasons which masked both the association between HbA1c and duration of diabetes with cataract in our study.

In our study, results showed that prevalence of cataract was insignificantly a bit higher in females than males (28% vs. 22%). In line with this, several case control studies have found that the excess risk of cataract among women persists after controlling for other risk factors. It is believed that productivity and female hormones play an effect (Johnson et al, 1998). Female gender was found to be associated with cataract among a Korean sample of diabetics (Kim S and Kim S.J., 2006) and another sample in UK (Janghorbani et al, 2000). Similar results were found in India (Cecile, et al, 2000).

In the present study, clinical settings were not found to be associated with cataract. This could have emerged due to different interacted diabetic and non-diabetic cataract risk factors. In line with this, the findings of one of the largest cataract studies that investigated 14 cataract risk factors showed that low socio-economic status, illiteracy, history of diarrhea, myopia, smoking and cheap cooking fuel were found to be associated with cataract development among an Indian population (Ughade et al, 1998). Additionally, In India, an increased risk of cataract was found for brown irises, smoking and use of oral corticosteroids (Cecile D, et al, 2000). Moreover, Melbourne and Framingham studies have reported twofold to threefold increase in cataract prevalence among subjects with affected siblings for cortical and nuclear/ subcapsular cataract respectively. Authors suggested that there is clustering of lens opacities within families. The clustering may be due to genetic factors, however, the role of environmental factors can not be excluded, (Fu et al, 1999, Darrow et al, 1994). However, the harmful effects of diabetes on the eye lens have been studied objectively. Rowe et al, reported that glycosilation of lens cortical proteins has been found to be significantly higher in diabetic patients with age-related cataract than in non-diabetic age-related cataract. Also, levels of malonicdialdehye (MDA) which is a major breakdown product of lipid were found significantly higher in diabetic cataract compared with clear lens and non-diabetic cataract (Rowe et al, 2000).

6.3.3 Effect of diabetic eye risk factors on glaucoma development:

Prevalence of glaucoma has been studied extensively by different studies. However the case definition of glaucoma has varied widely and clinical classification has not been consistent between studies. Intra-ocular pressure, optic nerve head features, visual field abnormalities and the different classifications of glaucoma make it difficult to compare prevalence and determinants between epidemiological studies (Allingham et al, 2005). However, the most appropriate available findings from literature were explored to better explain the present study findings. In our study, prevalence of glaucoma was found to be 9.5%. It was higher than the findings found in India (6%) despite the majority of the Indian participants (84%) presented for examination because of defective vision they had (Sharma, 1996). In aforementioned Al Ain study, prevalence of advanced diabetic eye complications (vitreous hemorrhage, retinal detachment and glaucoma) was found to be 1.7% (Maskari and Elsadig, 2007). It was also less than glaucoma prevalence by itself

among our study patients. Prevalence of glaucoma in the present study was found in higher proportions than it was found in Sweden (4.5%), (Olafsdottir et al, 2007) and in Australia (5.5%), (Mitchell et al, 1997). The higher prevalence of glaucoma (9.5%) among the present study comparable with the aforementioned studies could be possible due to the severity of diabetic eye risk factors among Palestinian diabetics. However, it could be due to different methodological approaches. In the present study, glaucoma was found to be significantly associated with HbA1c levels. However, it did not sustain its significance in the multivariate regression model except for the highest HbA1c level (9.2-13.2). Similarly, in Netherlands, Dielemans I et al found that high levels of blood glucose among diabetics was found associated with both elevated IOP (intra ocular pressure) and high-tension glaucoma (Dielemans et al, 1996).

In the aforementioned study by Negi and Vernon, they reported that patients with narrow-angle glaucoma are more likely to have abnormal glucose tolerance than healthy controls (Negi and Vernon, 2003). Uncontrolled blood glucose level induces eye lens enlargement which narrows the anterior chamber of the eye leading to increase intra ocular pressure (Kanski, 2003). None of the determinants listed in table (5.13) was found to be significantly associated with glaucoma. However, there was a trend increase of glaucoma cases with longer diabetes duration, older in age and hypertension. Comparably, Klein et al, in a 10 years cohort study, found that duration of diabetes was not an independent determinant of glaucoma.

Unlike our findings, they found that older in age was significantly related to increased incidence of glaucoma in both types of diabetes (Klein et al, 1997). Allingham et al, through their analyzing different glaucoma studies concluded that age is one of the strongest risk factors for different glaucoma types. Age was found associated with eye structure changes which precipitate different glaucoma types (Allingham et al, 2005). In the present study, there was no marked difference between glaucoma patients (mean SD= 60.9, 7.37) years and non-glaucoma patients (mean SD=58.4, 9.47) years in regard to age. Moreover, it is possible that different glaucoma risk factors could alter the significant association between glaucoma and age among our study patients.

Regarding hypertension, our findings revealed a non-significant trend increase in glaucoma cases in the presence of hypertension. Similarly, Charliat et al, found that high blood pressure was not associated with primary open angle glaucoma. The results indicated a strong genetic influence in the development of the disease (Charliat et, 1994). Opposite to our findings, Perruccio et al, found that significant increase in age-specific prevalence of glaucoma was found to be associated with hypertension (Perruccio et al, 2007). In a more detailed study, Algra et al, found that the magnitude of change in intra-ocular pressure (glaucoma main feature) with change in blood pressure is small. However, high systolic blood pressure was found to be correlated with open angle glaucoma. Prevalence of glaucoma increased significantly with higher quartiles systolic blood pressure compared with lower quartiles systolic blood pressure. Similar to systolic blood pressure, diastolic blood pressure was also found positively correlated with increased intra-ocular pressure.

Overall, hypertensive patients had 50% to 100% higher risk for glaucoma than normotensive patients (Algra et al, 1995). Conversely, Deokule and Weinreb concluded that the association between the incidence of primary open angle glaucoma and hypertension is an inverse one. It is the hypotension which increases the risk of primary open angle glaucoma. Arguably, low blood pressure negatively affects ocular blood perfusion (Deokule and Weinreb, 2008). In line with this, Allingham et al, reported that the literature has found confusing results regarding the association between blood pressure and glaucoma. It may be that both high and low blood pressures are linked to glaucoma. This explains the contradictory findings regarding the association between the two diseases. However, the best estimation of the effect of blood pressure on glaucoma comes from diastolic blood pressure perfusion measurement (subtracting intraocular pressure readings from blood pressure readings). There is a good evidence that a value of diastolic blood pressure perfusion of less than 55 mmHg is an important risk factor for glaucoma (Allingham et al, 2005). In line with this, the scope of the resent study and methodological approaches were beyond such investigation to show a realistic association between hypertension and glaucoma. For clinical settings, the results of the present study showed no significant association between clinical settings and glaucoma. As explained earlier, Allingham et al, stated that glaucoma is of many types and classifications, there are different glaucoma risk factors other than diabetes including family history, optic nerve head features, myopia and endocrine disorders (Allingham et al, 2005). Such multi-dimensional risk factors could mask the association between glaucoma and clinical settings in the present study. However, diabetes appears to have an effect on glaucoma development. One of the strongest published articles regarding the association of diabetes mellitus with primary open-angle glaucoma is the meta-analysis study by Bonovas et al (five case-control studies and seven cross-sectional studies between 1987 and 2001). The study concluded that diabetic patients are at significantly increased risk of developing primary open-angle glaucoma (Bonovas et al, 2004). In line with this, proper diabetic eye screening including glaucoma investigation is required.

6.3.4 Effect of diabetic eye risk factors on visual impairment:

In the present study, prevalence of "visual impairment" was found to be 35.7%. It was higher than the findings found by the Jordanian aforementioned study by Till et al (10.1%**),** (Till et al, 2005). This is might be due to that our study subjects were an eye clinic attendants while the Jordanians were a diabetic clinic patients. Regarding blindness, our study participants showed a lower blindness prevalence (5.4%) than the Jordanian patients (7.4%). This might be due to that blind people tend to participate in blindness investigations and research papers; which raised the Jordanian study prevalence of blindness. Till et al, reported that blind people are usually overwhelmed with visual care researches and new blinding related care investigations (Till et al, 2005). In USA, the Wisconsin Epidemiologic Study of Diabetic Retinopathy found that visual impairment was found to be 13% (Olafsdottir et al, 2007). A prevalence of blindness and visual impairment was found to be 1.2% and 7% respectively among a diabetic sample in France (Delcourt et al, 1995). It was much less than our study findings. While this is probably due to methodological variations, however, the high prevalence of visual impairment in our study could be due to the high magnitude of diabetic eye risk factors among our study participants.

Our study results showed that both age and duration of diabetes were found associated with visual impairment. Similarly, in Jordan, Sweden and UK, age and duration of diabetes were found associated with visual impairment (Till et al, 2005, Olafsdottir et al, 2007 and Bayer et al, 2000). In line with this, Bayer et al reported that retinopathy and cataract are both associated with increased age and longer diabetes duration. Thus, increased age and duration of diabetes are associated with poor vision (Bayer et al, 2000). Additionally, age is a risk factor for different diabetic eye conditioned mainly retinopathy. Longer in age is associated with longer duration of diabetes mellitus and more exposure to diabetic eye risk factors. This in turn exerts devastating effects upon the eye structure and functions over time (Johnson et al, 1998). In the present study, hypertension was found to be associated with visual impairment. Similar findings were found by the UKPDS study. Hypertension among diabetics was found to be a risk factor for visual impairment. Results showed a 47% reduction in visual acuity loss among patients having controlled blood pressure (Donnelly et al, 2000), (Genuth et al, 2002). In aforementioned study conducted by Olafsdottir E et al, similar to our findings, blood pressure was found significantly associated with best corrected visual acuity among diabetic patients (Olafsdottir et al, 2007). Additionally, the absolute risk of blindness in one eye for the tight blood pressure control group (3.1 per 1000 patient/years) was much lower compared with less tight blood pressure control group (4.1 per 1000 patient/years). The retina has no functioning sympathetic nerve fibers in patients with poorly controlled diabetes mellitus, blood flow is increased and auto-regulation is impaired. Stress of the high blood pressure will damage vessel walls and will precipitate and worsen retinopathy and related visual outcomes. Hence, blood pressure should be kept below 130/85mmhg (Matthews et al, 2004 and Genuth et al, 2002).

In our study, there was no significant association between gender and visual impairment. Conversely, Till et al, found that females were significantly more visually impaired than males among the Jordanian diabetics. Similar results have been reported from the United States, Europe and Arab world in which females were found more prone to visual impairment than males (Till et al, 2005, Olafsdottir et al, 2007 and Bayer et al, 2000). In the present study, as shown in part (5.5), there was no significant variation among both sexes in regard to the diabetic eye risk factors that were investigated. However, male gender was found to be associated with retinopathy, but not with either cataract or glaucoma. In line with this, more investigations in a boarder aspect to elucidate the determinants of visual status among Palestinian diabetics in regard to gender would be sensible and worthwhile.

For HbA1c, similar to our study findings, the level of glycemic control did not show statistical association with visual impairment as found by the aforementioned studies in Sweden and UK (Olafsdottir et al, 2007 and Bayer et al, 2000). In line with this, the majority of our study participants have shown higher levels of HbA1c than the recommended target. It is probably that they experienced higher levels of blood glucose prior to data collection phase of this study. Hence, this resulted in the absence of association between visual status and blood glucose levels. More precisely, HbA1c reading value did not show a marked difference between visually impaired subjects (mean, SD= 8.4, 1.61) and non-visually impaired patients (mean, SD= 8.2, 1.75). Therefore, it is of great value to improve diabetic management for the aim of improving blood glucose

control among Palestinian diabetics so as to preserve sight on the public health spectrum. In line with this, the results of the largest studies of UKPDS (Prospective Diabetes Study-UK) and the DCCT (Diabetes Control and Complications Trial-America) have provided further support for the American Diabetes Association's guidelines of a target HbA1c goal 7.0% for persons with diabetes (Klein, 2002). Diabetic complications are linked to poor glycemic control. Involvement of the retinal central vision of fovea by oedema and hard exudates is the most common cause of visual impairment in patients with diabetes. Diffuse maculopathy, clinical significant maculopathy, and other different forms of diabetic maculopathy are all visually impaired complications in which diabetic patients experience even in early stages of retinopathy. Neovascularisation of the eye retina in advanced stages of retinopathy leads to retinal ischemia, vitreous and retinal detachments which ended up with visual impairment and blindness (Kanski, 2003).

In the present study, Hebron clinic was statistically significantly associated with visual impairment. As shown in part (5.5), duration of diabetes was significantly higher associated with Hebron clinic rather than outreach clinic. Moreover, as shown in tables (5.6) and (5.9), Hebron clinic patients were significantly at increased odd of having diabetic eye complications (as a whole) and retinopathy compared with outreach patients. Such findings could have made the difference between Hebron clinic and Outreach regarding visual impairment. However, unlike Hebron clinic which provides primary and secondary eye care; outreach mobile clinic reaches patients in their communities to provide diabetic eye screening even if patients do not suffer from visual defects. It is possible that Hebron clinic patients; due to different reasons, did not present for eye care and check up unless they suffered from visual defects. Such argument is supported by the fact that among Hebron clinic patients, only 12.1% were found free from diabetic eye diseases, comparable with 29.6% of outreach patients, table (5.6). In UK, Lewis et al, investigated the determinants of attending eye care settings and the impact on visual acuity, the findings showed that eye clinic attendants consider eye clinics as a service for sick people rather than for normal eye checkup. Degree of awareness, clinic waiting time, norms and social factors are all of different effects on attending hospital eye clinics. Providing more complete information about diabetic eye complications and making eye clinics more convenient, would enhance the turn over of diabetic patients for regular eye examinations (Lewis et al, 2007). In line with this, diabetic patients in Palestine need to be encouraged and educated for better utilization of eye care settings for the sake of early and regular eye examination to better preserve sight.

6.4 Diabetic eye complications and their association with visual impairment among the study participants

In the present study, prevalence of visual impairment was found to be 35.7%. Diabetic retinopathy, cataract and glaucoma as exclusive single causes contributed to 31.3%, 6.0% and 0.7% of visual impairment respectively. Cataract and diabetic retinopathy as an exclusive combined cause, accounted for the highest share of visual impairment (36.7%). 10.7% of visual impairment was due to multiple causes of the main diabetic eye complications. 14.7% was as a result of a combination of the main diabetic eye complication/s associated with other eye co-morbidities**.** In line with this, Taylor H, reported that the challenge with cataract is to provision of cataract surgery that is available,

accessible and affordable is of great importance in eliminating avoidable blindness (Taylor, 2005). Hence, improving cataract eye services through improving accessibility and affordability of surgical cataract would improve visual status among diabetic patients and minimizes the burden of visual impairment in the Palestinian community. Additionally, Janghorbani et al, reported that, delaying the development of cataract formation through better management of diabetes remains the preferred approach. Accurate information regarding the incidence of cataract and associated risk factors in people with diabetes is important in planning a well-coordinated approach to this public health problem (Janghorbani et al, 2000 and Murphy, 1995). The increasing number of individuals with diabetes worldwide suggests that diabetic retinopathy will continue to be one of the major contributors to vision loss. Better control of preventable risk factors like hypertension, blood glucose levels, early detection and intervention are all sharp tools in delaying the onset of diabetic eye complications mainly retinopathy (Karadeniz and Yilmaz, 2007 and Johnson et al, 1998). In line with this, in our study, retinopathy contributed to 31.3% and 36.7% of visual impairment as a single cause and combined with cataract respectively. The high magnitude of retinopathy on visual impairment among the present study necessitates careful attention and better management of diabetes in the Palestinian community. While glaucoma is a serious sight threatening diabetic complications; in the present study, glaucoma contributed to 0.7% of visual impairment. This is possible due to that glaucoma patients were under medical follow up for both glaucoma and diabetes which resulted in better management of glaucoma. In line with this, Klein BE et al, reported that glaucoma diagnosis and identification tend to be better among diabetics than in the general community subjects as diabetic patients are usually followed up in way better than non-diabetics (Klein et al, 1997). The above discussion showed that the chief protective factor in preventing and delaying diabetic eye complications and visual impairment was attributed to control of diabetic eye risk factors. The establishment of national diabetic care programs in coordination with different care givers is vital to limit the deteriorating impact of diabetic eye complications among Palestinians. Olafsdottir E et al, concluded that the prevalence of low vision was no greater in the diabetes group than in the control group if there was strict control of diabetic eye risk factors and proper timely screening (Olafsdottir et al, 2007). In respect with this, it is important for health care settings to pay more attention to diabetic groups so as to prevent visual loss not merely from diabetic retinopathy but from other diabetic eye complications like cataract and glaucoma. The public health value of intervention programs to lower the risk of diabetic eye complications becomes more urgent as the incidence of diabetes mellitus is growing alongside the increase in life expectancy in Palestine.

Regarding diabetic eye complications (diabetic retinopathy, cataract and glaucoma) the literature has shown different determinants that have a marked influence on them other than diabetic eye risk factors. Hence, the reader should bear in mind that in our study the effect of diabetic eye risk factors on the diabetic eye complications could have been confounded by a complex of interrelated variables like genetic, environmental, occupational and different systemic pharmacological determinants.

6.5 Systemic diabetic complications

While investigating systemic diabetic complications is as important as looking into diabetic ocular complications, it was beyond the scope of the current study due to logistic limitations. However, the author tried to look into some of the available end stage systemic diabetic conditions among the study patients. This is primarily to provoke the readers to the ever existence of such dramatic diabetic effects. Hence the reader should keep in mind that the presented figures in our study, in no way reflect the magnitude of the systemic diabetic complications in our study.

The present study showed that only 0.7% of patients have had end stage renal diseases. However, such low prevalence does not actually reflect the magnitude of renal dysfunction among our study patients due to the fact that diabetic kidney disease is heterogenous and asymptomatic at certain stages. More precisely, renal dysfunction starts with the development of microalbuminuria as one of the first clinical signs of the classical course of diabetic nephropathy. This is followed by macroalbuminuria which progresses to glomerular filtration disturbances and eventually to end stage renal diseases (Yokoyama et al, 2009). Hence, due to our study limitations, it was not possible to collect the renal function profile for our patients which led to underestimation of renal problems among our study participants. In Japan, Yokoyama et al investigated renal dysfunction among a sample of type 2 diabetic patients. They found that the proportion of subjects with low glomerular filtration was 14.9% among those with microalbuminuria, 47.3% among those with macroalbuminuria and surprisingly 11.4% among those with even normoalbuminuria. They further concluded, that in diabetic patients who are even without albuminuria, it is reasonable to screen for glomerular filtration dysfunction (Yokoyama et al, 2009). In line with this, appropriate laboratory tests for early diagnosis of the degree of kidney dysfunction among Palestinian diabetics are of great importance in terms of better diabetic management approaches for the sake of hindering diabetic ocular and systemic complications.

6.6 Methodological considerations

The strength of the study comes from the fact that it was the first research paper which has ever shed the light on certain diabetic eye characteristics among Palestinian diabetics. Moreover, the core part of the present study data (diabetic eye complications, visual acuity) was collected based on objective testing. It was collected by ophthalmic trained staff using standardized examination equipments rather than self-reported. Therefore, the study recommendations would represent an insight to health care givers in adopting better diabetic care approaches in Palestine. Moreover, the study underpins further more detailed studies in exploring the effect of diabetic eye risk factors and the proper measurements for saving sight. However, the study was a cross-sectional, exploratory in nature; such methodological approach is appropriate for assessing the prevalence of risk factors and outcomes. More precisely, it examines the relationship between different variables at a point of time for a selected population rather than examining cause effect relationship-the case of intervention studies. Additionally, our sample was not representative to the whole

diabetic patients in Palestine. Rather it consisted of selected clinic attendants who most probably have had visual defects. Therefore, the findings of the study, in no way could be generalized to the whole diabetic patients in Palestine. St John eye hospital clinics, usually work during the morning hours of the day rather than around the hour. This could bias our sample because men usually are at their work places. Additionally, some patients with different physical and social conditions might not have had the opportunity to attend our clinics which in turn could be another source of selection bias.

6.7 Conclusions

This study, for the first time in Palestine, described the effects of diabetic eye risk factors on the development of diabetic eye complications and their impact on visual status among a diabetic sample. The study findings will underpin future diabetic eye care approaches and health care strategies by different health care sectors. It further represents a baseline for more detailed future research papers and comparisons. Based upon the present study findings, we can conclude the followings:

- Our study findings, in comparison with related findings elsewhere, showed a higher prevalence of both diabetic eye diseases and visual impairment.

- The majority of our sample showed uncontrolled blood glucose levels, only 22.6% of subjects have had within normal value range HbA1c (7 or less). Therefore, this was most probably the cause behind the absence of association between HbA1c and the diabetic eye complications among our study participants because HbA1c reflects the level of blood glucose for three months rather the whole period of diabetes duration. Hence, our study participants might have a longstanding above the normal HbA1c for a long time prior to data collection phase of the current study. Moreover, our study was deficient in the accurate classifications of the stages of diabetic retinopathy, cataract and glaucoma. This might have masked the association between HbA1c and diabetic eye complications since HbA1c was found to be associated with certain types of cataract, glaucoma and mostly with different levels of retinopathy including maculopathy.

- Associated hypertension was found in 39% of the study participants opposite to the findings elsewhere where the large majority of patients with type 2 diabetes are hypertensive. Regardless the fact that prevalence of hypertension in our study based on reporting rather than measurement, it is assumed that miss diagnosis of hypertension among our sample has existed. Hence some of patients did not have the proper anti-hypertensive treatment as they were not known of having the disease yet. It is expected that the actual prevalence of hypertension among our patients was underestimated.

- Prevalence of diabetic retinopathy among males was significantly higher (72.0%) than females, even though none of diabetic eye risk factors that were investigated in our study showed any significant association with male gender.

- Age, duration of diabetes, type 1 diabetes, hypertension, gender and clinical settings were all found significantly associated with participants who were found having diabetic eye complications compared with the non-diseased participants. In our study, all the

investigated diabetic eye risk factors were found to be associated with at least one of the diabetic eye complications or/and consequent visual impairment.

- Our results showed a high prevalence of diabetic retinopathy (66.6%) compared with relevant studies elsewhere, contributing to around one third (31.3%) of visual impairment among the study participants. Additionally, diabetic retinopathy was found to develop earlier among our study participants compared to published literature. 32.0% of the study participants have retinopathy with diabetes duration 0-5 years. However, under-diagnosis of diabetic cases could have been existed due to a long gap between the onset of diabetes and clinical diagnosis.

- More than one quarter (25.5%) of our study participants were found to have cataract. Cataract as a single cause or combined with retinopathy contributed to (42.7%) of visual impairment. Cataract was found to be strongly associated with age.

- Glaucoma was found to be of a markedly high prevalence (9.5%) in our study compared with the findings elsewhere. Glaucoma as a single exclusive cause occupied the least diabetic eye complication that contributed to visual impairment (0.7%). Arguably, this might be that glaucoma patients with diabetes usually undergo medical follow up more frequently than those without diabetes.

- In our study, prevalence of "visual impairment" was found to be 35.7%; higher than it was in other different studies in both developed and developing countries. While our results could be due to methodological variations; it could be due to the severity of diabetic eye determinants.

- Systemic diabetic complications were not examined thoroughly in the present study. Nephropathy could have been present at different stages among different patients in our study, even though patients were unaware of the disease as it is asymptomatic at certain stages. Similarly, one should realize the existence of diabetic neuropathy among our sample so as to be approached.

- The present study is of some limitations; smoking, education, income, family support and having medical insurance as determinants of diabetic eye complications were not investigated. Such determinants have been found to be associated with diabetic eye complications and related visual impairment by different epidemiological studies.

6.8 Recommendations

The results of this study can be utilized by different health care providers and planners in Palestine. Diabetes is a chronic disease of multi-systemic destructive effects; hence, controlling diabetic risk factors as well as diabetic eye complications are best approached through well organized diabetic care programs that are planned and implemented by different care givers at different levels. This is simply because diabetic risk factors, diabetic eye complications and diabetic systemic effects are inter-related and interacted. So, the recommendations of this study are in no means restrictedly addressed to St. John Eye

Hospital, rather to diabetic care providers and planners in general. Therefore, the following is recommended:

6.8.1 Implications for future ophthalmic research in Palestine:

1.Exploring the effect of other diabetic eye risk factors that have not been investigated like smoking, hyperlipidemia and dietary control will underpin more effective diabetic eye care approaches in Palestinian community.

2.Undertake qualitative research to identify the social and life style characteristics which hinder Palestinian diabetics from adopting preventive health care practices. This will positively address relevant health promotion approaches, enhance and encourage early detection, better blood pressure control, hampering health care barriers and better compliance with treatment regimen. Moreover, it further help in patients' empowerment towards preventive measures.

3.The best approach of identifying diabetic eye complications and related visual impairment outcome comes from a population-based study which no doubt will find out the determinants and prevalence of diabetic eye diseases and their visual impairment impact on the national level.

6.8.2 Implication for health care providers and planners:

- Diabetic care programs including diabetic eye care approaches should be addressed and prioritized from public health perspectives in the national health care strategies.

- General health diabetic care services, laboratory services and educational programs of different educational approaches should be addressed and well coordinated and collaborated by the different health care providers (government, NGO, UNRWA and private sector). Consequently, this will improve better identification of associated hypertension and earlier clinical diagnosis of diabetes among Palestinians. Moreover, it will address a holistic diabetic management including identification of systemic diabetic complications and ensures better control of diabetic eye risk factors so as to better minimize the development of diabetic eye complications.

- Better documentation of the medical, surgical and health practices information in the patients' individual medical records at St. John eye hospital.

- Enhance and uniform St. John eye hospital coding system of diagnosis at all hospital health care settings for better informative health information system and research purposes.

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Appendix (1) Data collection sheet

<table>
<tr><td colspan="10">Data Collection Sheet/ Diabetic Eye Diseases Study</td></tr>
<tr><td colspan="3">Case No.: .....

Date: …….

Card No…….</td><td colspan="3">Clinic:
1- Hebron center

2- Outreach clinic

District:……</td><td colspan="4" rowspan="5"></td></tr>
<tr><td colspan="6">Age:……...Sex: M F</td></tr>
<tr><td>VA</td><td colspan="2">Rt Eye</td><td colspan="3">Lt Eye</td></tr>
<tr><td>Unaided</td><td colspan="2"></td><td colspan="3"></td></tr>
<tr><td>Aided</td><td colspan="2"></td><td colspan="3"></td></tr>
<tr><td colspan="6">1-No Visual Impairment

2- Unilateral Low VA (ULV)

3- Bilateral Low VA (BLV)

4-Unilateral Blindness (UB)

5-Un. Low VA & Un. Blindness (ULV) + (UB)

6- Bilateral Blindness (BB)</td><td colspan="4"></td></tr>
<tr><td colspan="2">1-DM Type 1
2-DM Type 2</td><td colspan="2">Duration Of DM</td><td colspan="2">1- Not Hypertensive
2- Hypertensive</td><td colspan="2">HbA1c:</td></tr>
<tr><td colspan="6">Neuropathy:
1- None

2-Present or past facial palsy</td><td colspan="2">End stage Kidney problems:
1-No
2-Yes
Amputations:
1-None
2-Yes</td></tr>
<tr><td colspan="5">Main Causes of Visual Impairment</td><td colspan="5">Co-morbidities with/without “Main causes”</td></tr>
<tr><td>Diagn.</td><td>DR
-1-</td><td>Cataract
-2-</td><td>Glaucoma
-3-</td><td>None
9</td><td>Retinal Detach ./ vascular occlusions
-1-</td><td>Corneal opacity
-2-</td><td>Combined
-3-</td><td>Others
-4-</td><td>None</td></tr>
<tr><td>Unilateral</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Bilateral</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
</table>

Appendix (2): St. John Eye Hospital data collection instruments and tools

As per the hospital policy, the present study data was gathered using the following instruments:

- As per the hospital routine, patients' examination started with the supporting nursing staff. They opened a medical record for patients. This followed by documenting down the patient's personal details, chief complains, general health and ophthalmic history. Detailed information about medications, allergies, traumas were also clarified and documented.

  - **Snellen chart, measurement of visual acuity:**

    Visual acuity was measured by the supporting nursing staff using the universal valid standard Snellen chart at 6 meters distance. Vision for both eyes was taken separately. Unaided vision was simply measured without visual aids (like glasses). Vision is best measured using a standardised Snellen distance chart. It is read at 6 meters distance or at 3 meters distance using a smaller standard chart. Snellen chart consists of C letters which stands for the logarithm of the letter angle of resolution. Letters are of equal legibility with uniform spacing both between the same size letters in the same row and between the different rows. The chart should be read at 6 meters distance or equivalent distance according to the letters' size and related logarithm (Johnson et al, 1998).

  - **Eye glasses and Pin-hole: best corrected vision (aided):**

    Aided vision was measured with eye glasses if the patient has them already. A pin-hole was used to measure aided vision (best corrected) if the patient vision was less than 6/18 and patient has not got eye glasses yet. Pin-hole helps in assessing patients' visual acuity in the presence of refractive error. All patients who did not wear eye glasses and were found having vision less than 6/18 have had visual acuity test with pin hole. This allows to estimate the best corrected vision. The pin hole is an eye cover with tiny holes in the middle. It directs the light to be focused over the macula (the retinal part responsible for detailed and colour vision) once patient looks through the holes.

    The Pin-hole cuts out the need for refraction. Thus aided vision (best corrected vision) is estimated by testing vision with eye glasses if available or with a pin-hole (Johnson et al, 1998).

  - **Haag Streit slit lamp biomicroscope:**

    All patients were examined and underwent detailed eye examination. Examination of the anterior eye segment (orbital structure, cornea, iris, anterior chamber and lens) was carried out by the ophthalmologists using Haag Streit slit lamp.

Diagnosis of corneal opacities, cataracts, iris pathologies and anterior chamber pathologies were made and documented.

- **Applanation tonometry, an attached devise to the slit lamp:**

  Following anterior eye assessment, the intraocular pressure (tonometry) was measured using the applanation tonometry (a prism attached to the slit-lamp) to investigate glaucoma findings.

- **Eye Drops:**

  Tropicamide 0.5% and Phenylephrine HCl 10% eye drops were used to dilate the eye pupils. Dilation of the eye pupil is important so as to visualize the maximum area and the clearest view of the retina and optic nerve head.

- **Hand held magnification lens (90 and 78 diopters):**

  These magnifying optical lenses were used to help a better visualization and assessment of the eye posterior segment; retinal structure and optic disc.

For the Faith and in the Service of Humanity

ST. JOHN EYE HOSPITAL - JERUSALEM

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Research ethical committee
St John eye Hospital
Jerusalem

Dear Colleagues:
I am writing to you in request for your approval to conduct a study concerning diabetic patients that would be seen at the Hospital health care settings.
The study aims to identify causes of Blindness and visual impairment amongst diabetic patients that would attend the hospital health care settings (Base hospital, Hebron clinic and outreach) over a period of three months- between January 1st to March 31st 2007. This study will be conducted in partial fulfilment of a master Degree in "Public Health/Epidemiology" at Al Quads University.
The researcher will use routinely collected medical data documented by nurses and doctors, on completion the hospital staff will have full access to the results.
I hope this request will receive your approval.

Researcher: Khalilia Nasrallah Head of community health Dep.	Signature N. Khalilia	Date 19.12.06

Hospital Approval Statement:			
Signature	Position	Stamp	Date
	Nursing Director		19.12.06

Please support the St. John Eye Hospital Jerusalem which is a centre of excellence providing ophthalmic care of high quality and relevance to the people of the Holy Land irrespective of race, creed, social class and ability to pay.
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