Sudan University of Science and Technology

College of Graduate Studies

Study of Velocitymetry of Opthalmic Artery In Diabetic Pregnant Patients

دراسة سرعة جريان الدم في الشريان البصري لدى السيدات الحوامل المصابات بالسكري

A Thesis Submitted for Doctorate Philosophy Ph.D Degree in Diagnostic Medical Ultrasound

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الآيـة

قال تعالى :

(وَاللّهُ أَخْرَجَكُم مِّن بُطُونِ أُمَّهَاتِكُمْ لاَ تَعْلَمُونَ شَيْئاً وَجَعَلَ لَكُمُ السَّمْعَ

وَالأَبصَارَ وَالأَفْئِدَةَ لَعَلَّكُمْ تَشْكُرُو نَ).

صدق الله العظيم

سورة النحل الآية78

DEDICATION

To;

My parents...

My husband…

My Kids…

My Sisters and Brothers …

ACKNOWLEDGEMENT

I would like to thank God for enabling me to complete this thesis.

I would like to express my gratitude and thanks to my supervisor ***Dr. Alsafi Ahmed Abdallah*** *,the supervisor of my thesis for his continues help, supervision and guidance.*

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Abstract

The aim of this study was to assess velocitymetry of opthalmic artery in type(1)diabetic pregnant ladies and to characterize the ophthalmic artery perfusion in smoker pregnant ladies, diabetic pregnant ladies and smoker diabetic pregnant ladies using Doppler indices and to compare with normal healthy pregnancy.

Ultrasound examination for both eyes were obtained , Color Doppler Ultrasound High-frequency transducer 7.5MHZ , Voluson E6 machine was used in Al-Amin and Al- Ousrah poly clinic-Taif in Saudi Arabia. The data were collected using a data collection sheets. Data analyzed by (SPSS) program Version (16). Pregnant ladies with eye disease or pregnancy abnormality or preeclampsia were excluded.

In this study the sample was divided into two groups, group one, Inclusion criteria which included 15diabetic pregnant ladies, their ages ranged between (30-39), 14 healthy pregnant non diabetic ladies aged between (30-37), and 15 healthy non pregnant non diabetic subjects aged between (30-41) were selected as control group. group two subjects were divided into 4 groups: group 1 were normal healthy pregnant ladies (N=57) , group 2 were smokers pregnant ladies (N=44) ,group 3 were diabetic pregnant ladies (N=64),and group 4 were diabetic smoke pregnant ladies (N=71) ladies.

The result of this study revealed that:

Readings of Ophthalmic artery Doppler indices (resistive index (RI), pulsatility index (PI)) for type 1 diabetes ladies were found to be greater when compared with the control group values, and Mean Velocity (MV) was of lower values. The mean values ± SD were as follows: for right eye: resistive index, 1.3 ± 0.2 ($P < .005$ Control0.8 ± 0.1); pulsatility index, (3.6 ± 0.4 ($P < .005$Control1.6 ± 0.4); Mean Velocity (MV) 5.2 ± 1.1($P < .005$ Control 8.4± 3.2). For left eye resistive index, 1.4 ± 0.2 ($P < .005$ Control 0.7 ± 0.1); pulsatility index, 3.3 ± 0.5 ($P < .005$Control 1.6 ± 0.3); Mean Velocity (MV) 5.7 ± 0.8 ($P < .005$ Control 8.5 ± 3.2). The correlations between the variables and gestational age in the two pregnant groups were

studied and were compared with the control group and maternal treatment. The Doppler indices for right and left eyes differed significantly within the three trimesters for pregnant diabetic and pregnant non diabetic ladies when compared with the control group at p-value < 0.05

No significant difference was detected between the Doppler indices and the treatment taken as Diet Control, or insulin for type 1 diabetic pregnant ladies.

Significant increasing in resistive index, pulsatility index in the right and left eyes in all groups at p≤0.000 except in smoker pregnant ladies p≤ 0.069 , the PI decreased in the third trimester, and the Mean Velocity decreased significantly with advancing gestational age. A significant differences were detected between norms and the three groups at p≤0.000

The study concluded that Color Doppler Ultrasonography is useful for assessing blood flow.

Ophthalmic arteries Doppler Indices were affected significantly in pregnant ladies with or without type 1diabetes.

Smoking provokes perfusion changes in ophthalmic artery in smoker pregnant ladies. Thus, there are signs of an Ophthalmic artery vasoconstriction and hypoperfusion . Ophthalmic artery blood flow velocity was decreased in diabetic pregnant ladies.

The study suggested some recommendations and future studies which could be useful in this domain.

المستخلص

تهدف هذه الدراسة لتقويم مؤشرات دوبلر للشريان البصري في مرض السكر من النوع 1 لدي السيدات الحوامل. بالإضافة إلى توصيف الضخ في الشريان البصري لدي السيدات الحوامل المدخنات والسيدات الحوامل المصابات بمرض السكر باستخدام مؤشرات دوبلر والمقارنة مع الحوامل اللائي يتمتعن بالصحة الطبيعية.

تم فحص وتقويم كلتا العينين اليمنى واليسرى لكل المجموعات أثناء فترة الحمل بمؤشرات دوبلر، باستخدام جهاز الموجات فوق الصوتية (Voluson E6) عالي الكثافة النقطية بمقدار 7.5 ميقاهيرتز.بمستشفى الأمين والأسرة الطبي بالطائف-المملكة العربية السعودية. كان تجميع البيانات بواسطة نموذج جمع البيانات وحللت بواسطة برنامج التحليل الاحصائي (SPSS) نسخة (16). تم استبعاد السيدات المصابات بمرض العيون، أو شذوذ الحمل أو بمرحلة ما قبل التشنج الحملي.

تم تقسيم هذه الدراسة إلى مجموعتين، المجموعة الأولى : كانت معايير الإدراج 15 سيدة حامل مصابة بمرض السكر، وكانت أعمارهن تتراوح بين (30 -39) سنة، و14 سيدة حامل يتمتعن بالصحة ومن دون الإصابة بمرض السكر تتراوح أعمارهن بين (30 – 37) سنة، و 15 سيدة غير حامل يتمتعن بصحة جيدة ومن دون مرض السكر وتراوحت أعمارهن بين (30 – 41) سنة. وعليه فقد تم اختيارهن كمجموعة ضبط.

المجموعة الثانية: قسمت إلي أربعة مجموعات: وكانت المجموعة 1، السيدات الحوامل اللائي يتمتعن بالصحة الطبيعية (N=57)، و كانت المجموعة 2 للسيدات الحوامل المدخنات (N=44)، وكانت المجموعة 3 للسيدات الحوامل بمرض السكر (N=64)، وكانت المجموعة 4 للسيدات الحوامل المدخنات والمصابات بمرض السكر (N=71).

النتائج لهذه الدراسة كشفت عن الآتي:

كانت قراءات مؤشرات دوبلر للشريان البصري (مؤشر مقاوم RI، مؤشر النبضPI، للسيدات المصابات بمرض السكر من النوع 1 قد تم الحصول عليها بمقدار أكبر عندما تم مقارنتها مع قيم مجموعة الضبط وكانت السرعة المتوسطة MV بقيم أدني. وكانت القيم المتوسطة SD± على النحو التالي: بالنسبة للعين اليمنى: مؤشر مقاوم RI ، (0.1 ±0.8 Control 0.005> P) 0.2 ± 1.3

مؤشر النبض PI، (0.4 ± 1.6 Control .005 > P) 0.4 ± 3.6

السرعة المتوسطة MV، (3.2 ± 8.4 Control .005> p) 1.1 ± 5.2

بالنسبة للعين اليسرى مؤشر مقاوم RI، (0.1 ± 0.7 Control .005 > P) 0.2 ± 1.4

مؤشر النبض PI، (0.3 ± 1.6 Control .005> P) 0.5 ± 3.3

السرعة المتوسطة MV، (Control 8.5 ± 3.2 .005 > P) 5.7 ± 0.8 ، وعليه فقد تمت دراسة الارتباطات بين المتغيرات وفترة التكوين في مجموعتي الحوامل الاثنتين وتمت مقارنتها مع مجموعة الضبط ونوع العلاج المستخدم للسكر. وكشفت الدراسة بان مؤشرات دوبلر لكلتا العينين اليمنى واليسرى مختلفة بشكل ذي دلالة ضمن فترات الحمل الثلاث للسيدات المصابات بمرض السكر وغير المصابات بمرض السكر عند مقارنتهن مع مجموعة الضبط بقيمة p-value <0.05.

ولم يتم كشف أي اختلاف ذي دلالة بين مؤشرات دوبلر والمعالجة التي تم أخذها كحمية غذائية ، أو أنسولين للسيدات الحوامل المصابات بمرض السكر من النوع 1. أظهرت النتيجة زيادة ذات دلالة في مؤشرات المقاومة ومؤشر النبض لكلتا العينين اليمنى واليسرى في كل المجموعات بمقدار p<0.000 إلا لدي السيدات الحوامل المدخنات حيث كانت القيمة الدلالية p<0.069، ونقص مؤشر النبض في فترة الحمل الثالثة، بالإضافة إلي إن السرعة المتوسطة MV ناقصة بشكل ذي دلالة مع تقدم فترة التكوين. وتم كشف اختلافات ذات دلالة بين المعايير والمجموعات الثلاث بدلالة احصائية p<0.000

استنتجت الدراسة أن التصوير بالموجات فوق الصوتية الملونة مفيدا لتقويم تدفق الدم.

كان التأثير واضحاً على مؤشرات دوبلر للشرايين البصرية بشكل ذي دلالة عند السيدات الحوامل أو بدون الإصابة بمرض السكر من النوع1.

التدخين يحدث تغيرات في الضخ في الشريان البصري لدي السيدات الحوامل المدخنات. وهكذا، هنالك علامات تضيق في الأوعية و نقص الضخ في الشريان البصري. كما إن سرعة تدفق الدم في الشريان البصري كانت غير كافية لدي السيدات الحوامل والمصابات بمرض السكر.

اقترحت الدراسة بعض التوصيات والدراسات المستقبلية التي يمكن أن تكون مفيدة في هذا المجال.

List of Abbreviations

AION	Anterior ischaemic optic neuropathy
AMD	Age-related macular degeneration
BVA	Blood Velocity in the Ophthalmic Artery
CDI	Color Doppler Imaging
COex	carbon monoxide expired
CRA	Central Retinal Artery
CVD	CardioVascular Disease
DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
DR	Diabetic Retinopathy
EDV	End Diastolic Velocity
ETS	Environmental tobacco smoke
GA	Group A
GA	Gestational Age
GB	Group B
GC	Control Group
GD	Gestational Diabetes
HNS	Hyperosmolar nonketotic state
ICA	Internal Carotid Artery
IOP	Increased Intraocular Pressure

LTeye	Left Eye
Mv	Mean Velocity
NIN	Nicotine induced Nystagmus
OA	Opthalmic Artery
PCA	Posterior ciliary arteries
PDB	Post-delivery bleeding
PI	Pulsatility Index
PSV	Peak Systolic Velocity
PVD	Posterior Vitreous Detachment
RI	Resistive Index
RTeye	Right Eye
T1DM	Type 1 Diabetes mellitus
T2DM	Type 2Diabetes mellitus
TED	Thyroid Eye Disease
US	Ultra Sound
UV	UltraViolet
Vmax	peak velocity
Vmin	diastolic velocity

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Chapter one

Introduction

CHAPTER ONE

1.1 Introduction

Pregnancy can cause changes in the functioning of the eye in health and in disease and also affect preexisting ocular conditions especially in diabetic women, in which brings many changes that can lead to the development of diabetic retinopathy DR or worsening of pre-existing disease. In some patients this may develop into sight threatening disease which, if not treated adequately, can cause devastating visual impairment. (Taylor et al. 1999)

Progression of diabetic retinopathy occurs at least temporarily during pregnancy and postpartum. The pathogenic mechanisms of diabetic retinopathy progression during pregnancy are not fully understood. Several factors related to metabolic changes (hyper glycaemia), diabetes itself (duration of diabetes before conception, baseline status of diabetic retinopathy), pregnancy physiology (hypervolemia and hyper coagulation, impaired retinal auto regulation) and pregnancy complications (pre-eclampsia) seem to play important roles in the progression of diabetic retinopathy during pregnancy. On the other hand, systemic angiopoietin and vasoactive factors seem to have minor role in the deterioration of diabetic retinopathy during that time period. (Kaaja et al .2007)

Developments in medical, obstetrical, and ophthalmologic management of the pregnant diabetic (depending largely on careful monitoring) have greatly improved the prognosis for successful pregnancies and maintaining vision. (Kaaja et al .2007)

Color Doppler imaging method is useful for assessing blood flow in ocular circulation, as in ophthalmic artery which is mainly change in velocity in patients with diabetes, also blood flow in central retinal artery and short posterior ciliary arteries are also change and can be significant in the development of diabetic retinopathy.(Cristiana Alves de Oliveira et al.2012)

As observed during study smoking play an important role in accelerating retinopathy by losing elasticity of vessels and thus affecting the blood flow which can be detected using Doppler u/s.

Tobacco smoke is composed of at least 7000 active chemicals, most of them toxic and potentially damaging to the eye. (U.S.D.S.2010) .Smoking can cause or worsen several eye disorders, in particular Age-related Macular Degeneration (AMD), which may lead to blindness.(RNIB, 2013)

Klein et al, comparing the rate of progression of DR between a group of pregnant women with diabetes and a group of non-pregnant women with diabetes, found that the pregnant women had a significantly higher rate of progression after accounting for the influence of glycemia control and blood pressure.(.Klein BEK et al.1990) .Similarly, Moloney et al discovered that pregnancy increased both the incidence of DR and its rate of progression.

The aim of the present study was, therefore, to investigate blood flow changes during pregnancy in a group of healthy pregnant women in comparison with a group of pregnant women with diabetes, also to look for effect of factor of smoking in these groups and to relate these to changes in DR.

1.2 Problem of the study

Pregnant women with diabetes mellitus type 1 must carefully balance their food intake and their exercise to regulate their blood sugar levels, in an attempt to avoid hypoglycemic (low blood sugar) and hyperglycemic (high blood sugar) reactions, which can be life threatening.

Type 1 diabetes occurs when the body's immune system attacks and destroys certain cells ,These cells -- called beta cells. when the beta cells are destroyed, no insulin can be produced, and the glucose stays in the blood instead, where it can cause serious Damage to the body.

Over time, the high sugar levels in the blood may damage the nerves and small blood vessels of the eyes, kidneys, and heart a Doppler ultrasound studies of the blood vessels in the eyes in diabetic pregnant mothers is vital to determine the change of flow of these vessels.

Another factor can accelerate this effect in artery is smoking (nicotine) by decrease the flow velocity of these vessels may be due to an increase in the vascular resistance of the vessels in smokers. This may be important in patients with eye disease in whom altered blood flow already contributes to the ocular or orbital pathology. Also, the amount of oxygen in blood is also reduced with the corresponding increase in carbon monoxide.

The importance of Doppler u/s is to detect the change in blood flow in vessels occurred due to the above mentioned changes in the vessels nature.

1.3 Objectives

General objectives:

To study velocitymetry of opthalmic artery in pregnant diabetic and smoker mothers.

Specific objectives:

- Measure the change of flow of ophthalmic artery in diabetic mothers.(type1)(RI, PI, Mv) and trace the findings in first, second and third trimester .
- Evaluate the relationship between Doppler indices and duration of diabetes.
- To evaluate the Doppler indices in smoker pregnant ladies.
- To evaluate the Doppler indices in smoker diabetic pregnant ladies.

1.4 Overview of study

This study consisted of five chapters. Chapter one is an introduction which includes; problem and objective of the study. Chapter two is a literature review which includes; Anatomy, Physiology, Pathology and previous studies. Chapter three is about research methodology. In Chapter four the results are presented and Chapter five includes; discussion, conclusions and recommendations.

Chapter Two

Literature Review

CHAPTER TWO

Theoretical Background

2.1 Anatomy:

2.1.1 Parts of the Eye and Their Functions

The eye is one of the most complex parts of the body. The different parts of the eye allow the body to take in light and perceive objects around us in the proper color, detail and depth. This allows people to make more informed decisions about their environment. If a portion of the eye becomes damaged, you may not be able to see effectively, or lose your vision all together. (A.A.O et al.2001).

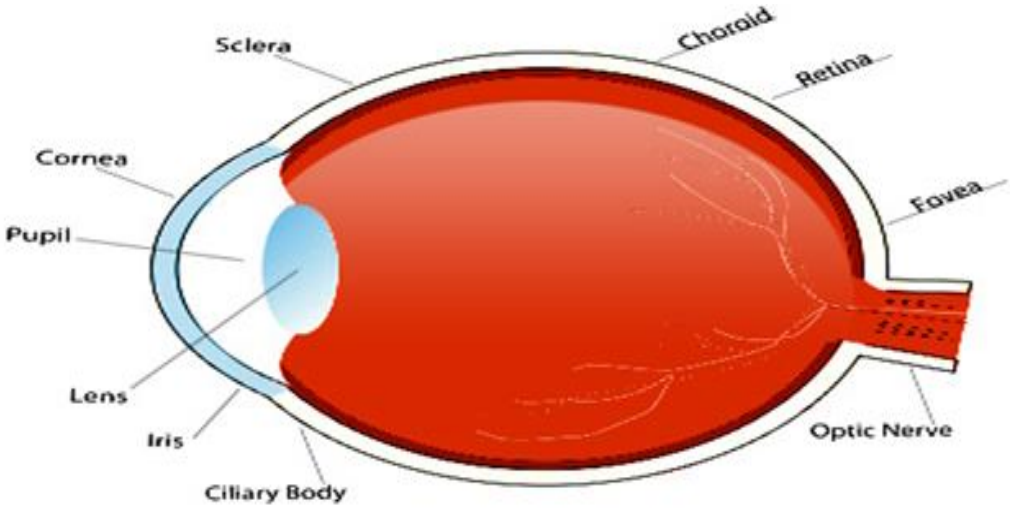

Fig. 2.1: parts of the eye.

(www.md-health.com)

There are several physical and chemical elements that make up the eye. The eye is also heavily involved with the nervous system, which allows the brain to take in information from the eyes and make the appropriate decisions on how to act upon this information. The nerves must be kept in prime condition or the brain may start to receive false images, or you will not take in enough information to get an accurate perception of your environment. (A.A.O et al.2001).

2.1.1.1 Cornea

The cornea is the outer covering of the eye. This dome-shaped layer protects your eye from elements that could cause damage to the inner parts of the eye. There are several layers of the cornea, creating a tough layer that provides additional protection. These layers regenerate very quickly, helping the eye to eliminate damage more easily. The cornea also allows the eye to properly focus on light more effectively. Those who are having trouble focusing their eyes properly can have their corneas surgically reshaped to eliminate this problem. (A.A.O et al.2001).

2.1.1.2 Sclera

The sclera is commonly referred to as the "whites" of the eye. This is a smooth, white layer on the outside, but the inside is brown and contains grooves that help the tendons of the eye attach properly. The sclera provides structure and safety for the inner workings of the eye, but is also flexible so that the eye can move to seek out objects as necessary. (A.A.O et al.2001).

2.1.1.3 Pupil

The pupil appears as a black dot in the middle of the eye. This black area is actually a hole that takes in light so the eye can focus on the objects in front of it.

2.1.1.4 Iris

The iris is the area of the eye that contains the pigment which gives the eye its color. This area surrounds the pupil, and uses the dilator pupillae muscles to widen or close the pupil. This allows the eye to take in more or less light depending on how bright it is around you. If it is too bright, the iris will shrink the pupil so that they eye can focus more effectively. (A.A.O et al.2001).

2.1.1.5 Conjunctiva Glands

These are layers of mucus which help keep the outside of the eye moist. If the eye dries out it can become itchy and painful. It can also become more susceptible to damage or infection. If the conjunctiva glands become infected the patient will develop "pink eye. (A.A.O et al.2001).

2.1.1.6 Lacrimal Glands

These glands are located on the outer corner of each eye. They produce tears which help moisten the eye when it becomes dry, and flush out particles which irritate the eye. As tears flush out potentially dangerous irritants, it becomes easier to focus properly. (A.A.O et al.2001).

2.1.1.7 Lens

The lens sits directly behind the pupil. This is a clear layer that focuses the light the pupil takes in. It is held in place by the ciliary muscles, which allow the lens to change shape depending on the amount of light that hits it so it can be properly focused.

2.1.1.8 Retina

The light focuses by the lens will be transmitted onto the retina. This is made of rods and cones arranged in layers, which will transmit light into chemicals and electrical pulses. The retina is located in the back of the eye, and is connected to the optic nerves that will transmit the images the eye sees to the brain so they can be interpreted. The back of the retina, known as the macula, will help interpret the details of the object the eye is working to interpret. The center of the macula, known as the fova will increase the detail of these images to a perceivable point. (A.A.O et al.2001).

2.1.1.9 Ciliary Body

Ciliary body is a ring-shaped tissue which holds and controls the movement of the eye lens, and thus, it helps to control the shape of the lens.

2.1.1.10 Choroid

The choroid lies between the retina and the sclera, which provides blood supply to the eye. Just like any other portion of the body, the blood supply gives nutrition to the various parts of the eye. (A.A.O et al.2001).

2.1.1.11 Vitreous Humor

The vitreous humor is the gel located in the back of the eye which helps it hold its shape. This gel takes in nutrients from the ciliary body, aqueous humor and the retinal vessels so the eye can remain healthy. When debris finds its way into the vitreous humor, it causes the eye to perceive "floaters," or spots that move across the vision area that cannot be attributed to objects in the environment. (A.A.O et al.2001).

2.1.1.12 Aqueous Humor

The aqueous humor is a watery substance that fills the eye. It is split into two chambers. The anterior chamber is located in front of the iris, and the posterior chamber is directly behind it. These layers allow the eye to maintain its shape. This liquid is drained through the Schlemm canal so that any buildup

in the eye can be removed. If the patient's aqueous humor is not draining properly, they can develop glaucoma. (A.A.O et al.2001).

Other parts of the human eye play a supporting role in the main activity of sight:

- Some carry fluids (such as tears and blood) to lubricate or nourish the eye.
- Others are muscles that allow the eye to move.
- Some parts protect the eye from injury (such as the lids and the epithelium of the cornea).

And some are messengers, sending sensory information to the brain (such as the pain-sensing nerves in the cornea and the optic nerve behind the retina) (A.A.O et al.2001).

2.1.2blood supply of the eye

The arterial supply to the orbit derives its origin from the internal carotid artery (ICA). In the head and the neck, the common carotid bifurcates at the C4-C5 region. This bifurcation leads to the external carotid artery and the ICA. The external carotid artery is an important vessel because of its blood supply to the orbit, dura, and cranial nerves. The important branches involved in irrigating the orbit include the following:

- Facial artery and angular artery branch - Supplies orbit and medial lid
- Occipital artery.
- Superficial temporal artery - Supplies frontal and superior orbit
- Internal maxillary artery.
- Middle meningeal artery - Major vessel supplying the orbit in the absence of the ophthalmic vessel.
- Anterior deep temporal and infraorbital artery.

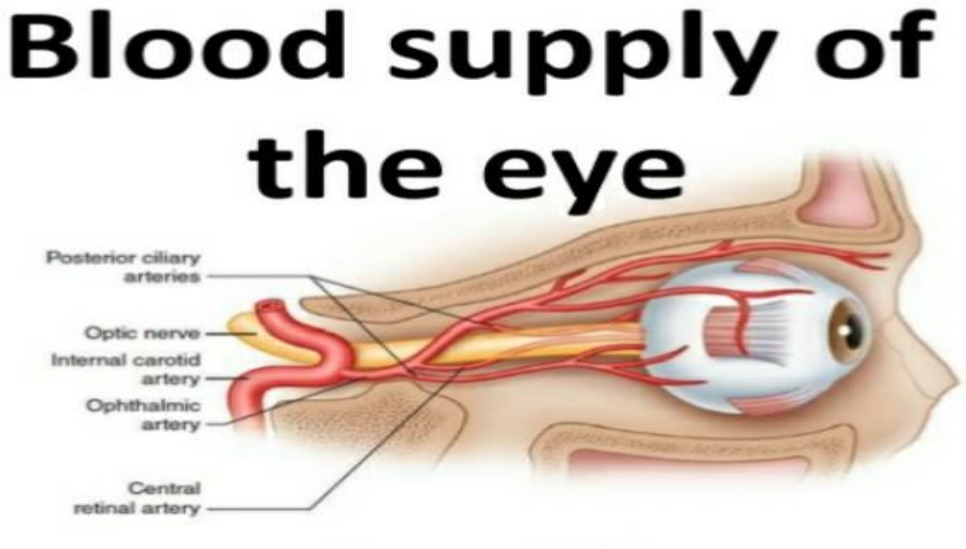

Fig. 2.2: blood supply of the eye
(www.doereport.com)

2.1.2.1 The Arterial System:

2.1.2.2Internal carotid artery

In addition to supplying the anterior part of the brain, eye, and adnexa, the internal carotid artery (ICA) sends branches to the forehead and the nose. The course and relations of this vessel may be divided into 4 portions: cervical, petrous, cavernous, and cerebral. The length of the ICA varies according to the length of the neck and the point of bifurcation of the common carotid. Although rare, it sometimes arises from the arch of the aorta. Instead of being straight, the course of the ICA is often very tortuous.(Hayreh SS et al 2006)

Branches from the ICA are numerous, and they are not within the scope of this article. This article primarily discusses the branches and the tributaries that irrigate the orbit. Interestingly, the cervical portion of the ICA gives off no branches. The ICA provides collateralization with the middle meningeal artery and lacrimal and ethmoidal anastomoses. (Hayreh SS et al 2006)

2.1.2.3 Ophthalmic artery

The ophthalmic artery (arteria ophthalmica) is the major blood supply of the orbit .It arises from the ICA (first branch of the ICA) as the ICA is emerging from the cavernous sinus on the medial side of the anterior clinoid process. It enters the orbital cavity through the optic foramen, below and lateral to the optic nerve. The ophthalmic artery passes over the nerve (in 85% of cases) to reach the medial wall of the orbit.(Hayreh SS et al 2006)

The artery then proceeds forward horizontally, beneath the lower border of the superior oblique muscle, and divides into 2 terminal branches, frontal and dorsal nasal. As the artery crosses the optic nerve, it is accompanied by the nasociliary nerve and is separated from the frontal nerve by the superior rectus muscle and the superior levator palpebral muscle. The ophthalmic artery rarely arises from the middle meningeal artery. Most branches of the ophthalmic artery arise in the posterior one third of the orbit and pass anteriorly. As outlined below, the branches of the ophthalmic artery are divided into an orbital group, distributing vessels to the orbit and surrounding parts, and an ocular group, distributing vessels to the muscles and bulb of the eye.(Hayreh SS et al 2006)

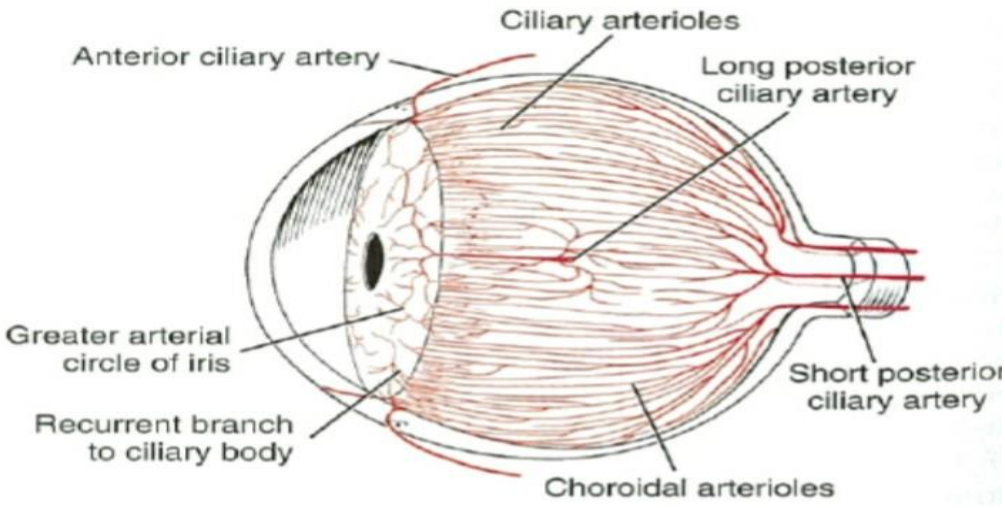

Fig. 2.3: Arterial system of the eye .

(www.graysanatomyonline.com)

2.1.2.4 Orbital group:

The orbital group consists of the following (see the image below):

- Lacrimal artery.
- Supraorbital artery.
- Posterior ethmoidal artery.
- Anterior ethmoidal artery.
- Internal palpebral artery.
- Frontal artery.
- Nasal artery.

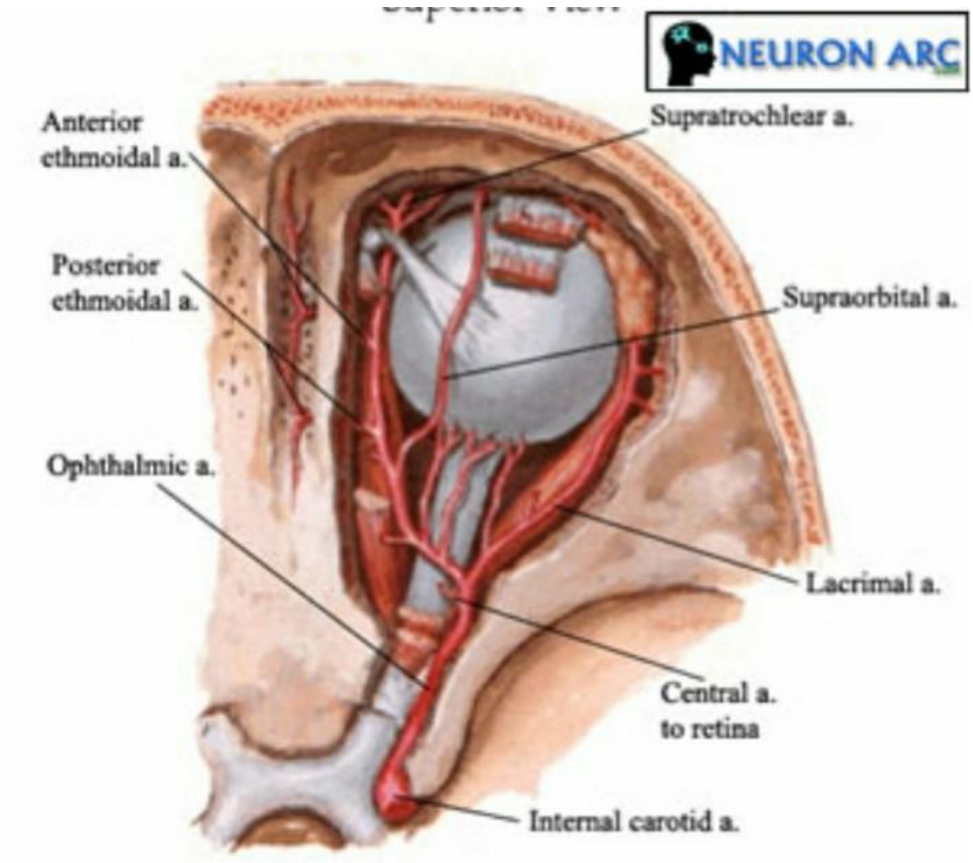

Fig. 2.4: Image show orbital group of the eye.

(www.emedicine.medscape.com)

2.1.2.4.1 Lacrimal artery

One of the largest branches derived from the ophthalmic artery, the lacrimal artery (arteria lacrimalis) arises close to the optic foramen and, not

infrequently, is given off before the ophthalmic artery enters the orbit. Interestingly, the lacrimal artery has a variable origin. .(Hayreh SS et al 2006)

This artery runs along the lateral wall of the orbit, accompanying the lacrimal nerve along the upper border of the lateral rectus muscle, and supplies the lacrimal gland.

The superior and inferior lateral palpebral arteries, which are terminal branches of the lacrimal artery, irrigate the upper and lower eyelids, respectively, and the conjunctiva. These vessels run medially and anastomose with the medial palpebral arteries, forming an arterial circle.(Hayreh et al SS. 2006)

The muscular branches of the lacrimal artery supply the superior and lateral recti muscles. The glandular branches irrigate the lacrimal gland.

The lacrimal artery may also give off 1 or 2 zygomatic branches. One zygomatic branch passes through the zygomatico-temporal foramen, to reach and irrigate the temporal fossa, and anastomoses with the deep temporal arteries. Another branch appears on the cheek through the zygomatico-facial foramen and anastomoses with the transverse facial artery.(Hayreh SS et al. 2006)

A recurrent meningeal branch of the lacrimal artery passes backward through the lateral part of the superior orbital fissure or through the meningeal foramen in the greater wing of the sphenoid bone, to the dura mater, and anastomoses with a branch of the middle meningeal artery. The lacrimal artery sometimes is derived from one of the anterior branches of the middle meningeal artery. This vessel establishes an anastomosis between the ICA and the external carotid artery.(Hayreh SS et al. 2006)

2.1.2.4.2 Supraorbital artery

The supraorbital artery (arteria supraorbitalis) arises from the ophthalmic artery, superiorly, as that vessel crosses over the optic nerve. The supraorbital artery passes upward on the medial borders of the superior rectus muscle and the levator palpebral muscle. The supraorbital nerve accompanies the supraorbital artery between the periosteum and the levator palpebral muscle to the supraorbital foramen. .(Hayreh SS et al 2006)

As the supraorbital artery passes through the supraorbital foramen, it divides into a superficial branch and a deep branch, which supply the eyebrow and the forehead. It anastomoses with the frontal artery, the frontal branch of the superficial temporal artery, and the supraorbital artery of the opposite side. Within the orbit, the supraorbital artery supplies the superior rectus muscle and the levator palpebral muscle. Furthermore, it sends a branch across the pulley of the superior oblique muscle to supply the medial palpebral commissure.(Hayreh SS. 2006)

2.1.2.4.3 Ethmoidal artery

The ethmoidal artery branches into the posterior and anterior ethmoidal arteries. The posterior ethmoidal artery, the smaller of the 2 branches, arises from the ophthalmic artery as it passes along the medial wall between the superior oblique muscle and the medial rectus muscle. This vessel passes through the posterior ethmoidal canal, supplying the posterior ethmoidal cells. In the orbit, this vessel can irrigate the superior oblique muscle, the superior and medial recti muscles, and the superior levator palpebral muscle. .(Hayreh SS et al 2006)

The anterior ethmoidal artery accompanies the nasociliary nerve and exits the orbit through the anterior ethmoidal foramen. In the orbit, it supplies the superior oblique muscle. This vessel also supplies the anterior and middle

ethmoidal cells, frontal sinus, lateral wall nose, and nasal septum.(Hayreh SS. Et al 2006)

2.1.2.4.4 Medial palpebral arteries

The superior and inferior medial palpebral arteries (arteriae palpebrales mediales, internal palpebral arteries) arise from the ophthalmic artery, opposite the pulley of the superior oblique muscle. These vessels leave the orbit to encircle the eyelids near their free margins, forming a superior arch and an inferior arch between the orbicularis oculi and the tarsi.

The superior medial palpebral artery anastomoses with the zygomatico-orbital branch of the temporal artery at the lateral angle of the orbit. This artery also anastomoses with the upper of the 2 lateral palpebral branches of the lacrimal artery. (Hayreh SS et al. 2006)

The inferior medial palpebral artery anastomoses with the lower of the 2 lateral palpebral branches from the lacrimal artery at the lateral angle of the orbit, as well as with the transverse facial artery and, at the medial part of the eyelid, with a branch from the angular artery. From this last anastomosis, a branch passes to the nasolacrimal duct, ramifying in its mucous membrane, as far as the inferior meatus of the nasal cavity. The superior and inferior medial palpebral arteries supply the lacrimal sac.(Hayreh SS et al.2006)

2.1.2.4.5 Frontal artery

One of the terminal branches of the ophthalmic artery, the frontal artery (arteria frontalis) leaves the orbit at its medial angle above the trochlea with the supratrochlear nerve, ascending on the forehead, and supplies the forehead and the scalp. The frontal artery anastomoses with the supraorbital artery and the contralateral vessels.(Hayreh SS et al.2006)

2.1.2.4.6 Dorsal nasal artery

The dorsal nasal artery (arteria dorsalis nasi, nasal artery), the other terminal branch of the ophthalmic artery, leaves the orbit above the medial palpebral tendon. After giving off a branch to the upper part of the lacrimal sac, it divides into 2 branches, one of which crosses the root of the nose. The dorsal nasal artery anastomoses with the angular artery, a terminal branch of the facial artery.(Hayreh SS et al.2006)

2.1.2.5 Ocular group:

The ocular group consists of the following:

- Long ciliary artery
- Short ciliary artery
- Anterior ciliary artery
- Central retinal artery
- Muscular artery group

2.1.2.5.1 Ciliary arteries

The ciliary arteries (arteriae ciliares) are divided into 3 groups: short posterior, long posterior, and anterior ciliary arteries.

The short posterior ciliary arteries may number 6-12 vessels. Arising from the ophthalmic artery or its branches, the short posterior ciliary arteries travel anteriorly around the optic nerve to the posterior part of the eyeball, piercing the sclera around the entrance of the nerve. They supply the choroid and ciliary processes.(A.A.O.2001)

The 2 long posterior ciliary arteries pierce the sclera posteriorly, a short distance from the optic nerve. They travel forward between the sclera and the choroid, to the ciliary muscle, where they divide into 2 branches. These branches form an arterial circle, the circulus arteriosus major, around the circumference of the iris.

Numerous converging branches from the circulus arteriosus major run in the substance of the iris to its pupillary margin, where they form a second arterial circle, the circulus arteriosus minor. The long and short posterior ciliary arteries give collateralization to all the recti muscles, except the lateral rectus muscle. (A.A.O.2001)

The anterior ciliary arteries are derived from the muscular branches. They travel to the front of the eye to form a vascular zone beneath the conjunctiva. They then pierce the sclera, a short distance from the cornea, and end in the circulus arteriosus major. The anterior ciliary arteries supply, in pairs, 3 recti muscles: superior, medial, and inferior. The lateral rectus muscle is supplied by a single anterior ciliary artery arising from the lacrimal artery.

Anterior to the insertions of the 4 recti muscles, the anterior and posterior ciliary arteries anastomose with the long posterior ciliary vessels where the anastomosed vessels pierce the sclera, forming the intramuscular circle of the iris. (A.A.O.2001)

2.1.2.5.2 Central retinal artery

The central retinal artery (arteria centralis retinae) is the first branch, as well as one of the smallest branches, of the ophthalmic artery. It arises in the posterior one third of the ophthalmic artery. The central retinal artery travels for a short distance beneath the optic nerve, entering the dural sheath of the optic nerve about 5-15 mm behind the globe. It pierces the optic nerve obliquely and travels forward through the central optic nerve. This artery is the principal blood vessel that irrigates the retina.(A.A.O.2001)

2.1.2.5.3 Muscular branches:

The muscular branches (rami musculares) arise from a common trunk, leading to the superior (lateral) branch and the inferior (medial) branch. The

muscular branches enter the sclera anterior to tendon insertions of the recti muscles and anastomose with the long posterior ciliary arteries.(A.A.O.2001)

The superior branch supplies the levator muscle, the superior rectus muscle, the superior oblique muscle, and a portion of the lateral rectus muscle (the lacrimal artery. The inferior branch supplies the medial rectus muscle, the inferior rectus muscle, the inferior oblique muscle, and, sometimes, the lateral rectus muscle. This vessel gives off most of the anterior ciliary arteries. Additional muscular branches are given off by the lacrimal and supraorbital arteries or by the trunk of the ophthalmic artery. All the recti muscles have 2 anterior ciliaries, except the lateral rectus muscle.(A.A.O.2001)

2.1.3 Blood supply to the eyelid:

The blood supply to the eyelid includes the following:

- Marginal arcade - Anterior to the tarsus
- Peripheral arcade - Between the levator muscle and the Muller muscle
- Lacrimal artery

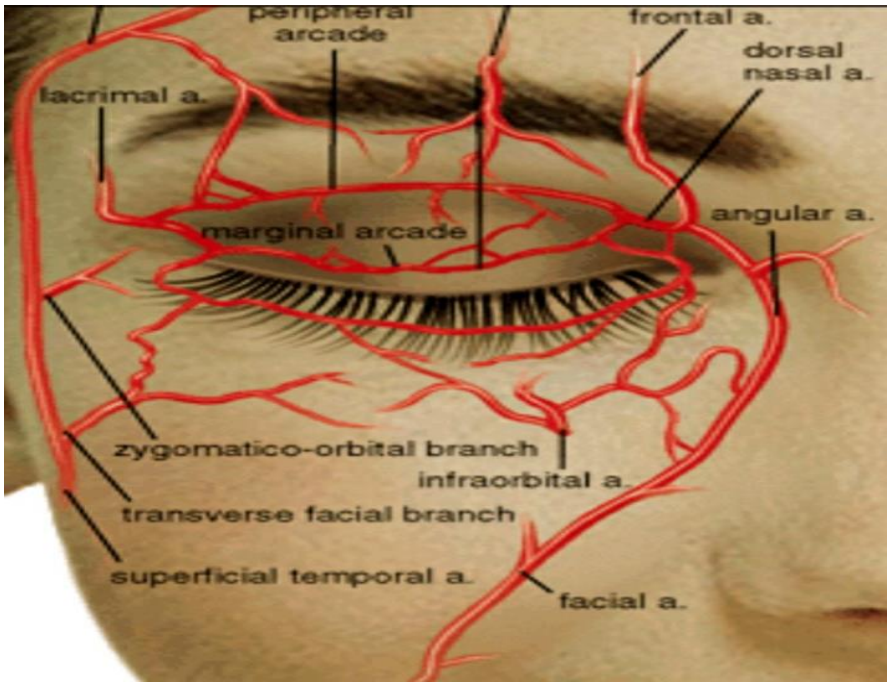

Fig. 2.5: Image show blood supply of the eyelid.
(www.slides share.net)

2.1.4venous system of the eye.

2.1.4.1 Vortex veins

The vortex veins provide drainage for the uveal tract (choroid, ciliary body, iris). They pierce the sclera obliquely and open posterior to the equator. The superior vortex veins (lateral and medial) drain into the superior ophthalmic vein or its muscular or lacrimal branches. The 2 inferior vortex veins (lateral and medial) drain into the inferior ophthalmic vein. (A.A.O.2001)

2.1.4.2 Superior ophthalmic vein

The superior ophthalmic vein is the main venous channel for the superior orbit; it drains to the cavernous sinus. The course of the superior ophthalmic vein begins at the inner angle of the orbit. It pursues the same course as the ophthalmic artery and receives tributaries corresponding to the branches of that vessel. It passes between the 2 heads of the lateral rectus muscle, through the medial part of the superior orbital fissure, and ends in the cavernous sinus.(A.A.O.2001)

2.1.4.3 Inferior ophthalmic vein

The inferior ophthalmic vein begins at the floor and medial wall of the orbit, travels backward, and divides into 2 branches. It provides a channel for inferior drainage. (A.A.O.2001)

2.2.Physiology of the eye:

2.2.1 Vision path way

Light rays enter the eye through the cornea, the clear front “window” of the eye. The cornea’s refractive power bends the light rays in such a way that they pass freely through the pupil the opening in the center of the iris through which light enters the eye. (Mitchel et al.2011) The iris works like a shutter in a

camera. It has the ability to enlarge and shrink, depending on how much light is entering the eye. (Morry 1999, Rita 2016)

After passing through the iris, the light rays pass thru the eye's natural crystalline lens. This clear, flexible structure works like the lens in a camera, shortening and lengthening its width in order to focus light rays properly.(Morry1999, Rita2016) Light rays pass through a dense, transparent gel-like substance, called the vitreous that fills the globe of the eyeball and helps the eye hold its spherical shape.

In a normal eye, the light rays come to a sharp focusing point on the retina. The retina functions much like the film in a camera. It is responsible for capturing all of the light rays, processing them into light impulses through millions of tiny nerve endings, (Morry1999, Rita 2016) then sending these light impulses through over a million nerve fibers to the optic nerve. Because the keratoconus cornea is irregular and cone shaped, light rays enter the eye at different angles, and do not focus on one point the retina, but on many different points causing a blurred, distorted image

In summary, the cornea is the clear, transparent front covering which admits light and begins the refractive process. It also keeps foreign particles from entering the eye.(Morry1999, Rita2016) The pupil is an adjustable opening that controls the intensity of light permitted to strike the lens. The lens focuses light through the vitreous humor, a clear gel-like substance that fills the back of the eye and supports the retina.

The retina receives the image that the cornea focuses through the eye's internal lens and transforms this image into electrical impulses that are carried by the optic nerve to the brain.

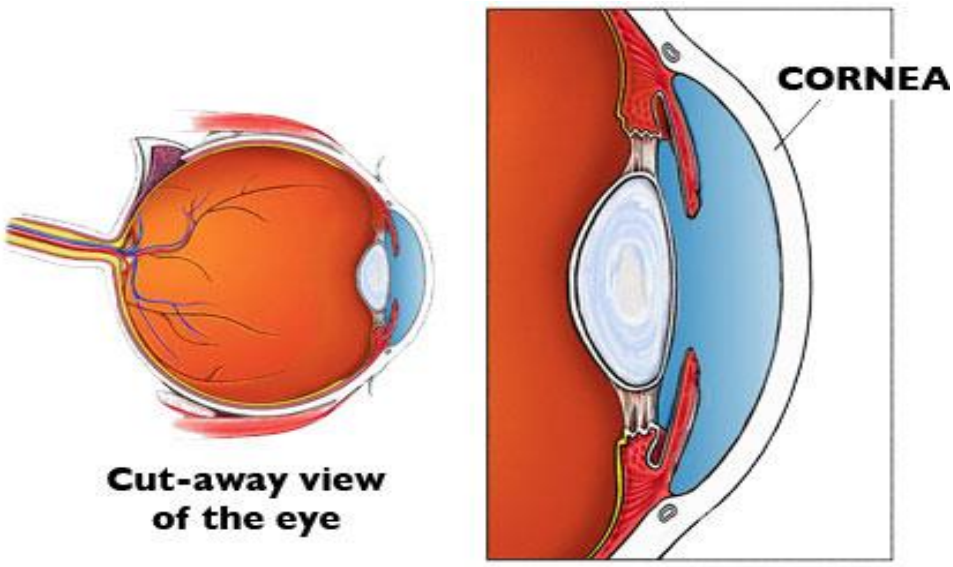

Fig. 2.6: work of the eye.

(www.nKcf.org)

We can tolerate very large scars on our bodies with no concern except for our vanity. This is not so in the cornea. Even a minor scar or irregularity in the shape can impair vision. No matter how well the rest of the eye is functioning, if the cornea is scarred, clouded or distorted, vision will be affected.

In keratoconus, the irregular shape of the cornea does not allow it to do its job correctly, leading to distortion of the image it passed to the retina and transmitted to the brain. (Morry1999, Rita2016)

2.2.2The Cornea

The eye is enclosed by a tough white sac, the sclera. The cornea is the transparent window in this white sac which allows the objects you are looking at to be carried in the form of light waves into the interior of the eye.

The surface of the cornea is where light begins its journey into the eye. The cornea's mission is to gather and focus visual images. Because it is out front, like the windshield of an automobile, it is subject to considerable abuse from the outside world. (Morry1999, Rita2016)

The cornea is masterfully engineered so that only the most expensive manmade lenses can match its precision. The smoothness and shape of the cornea, as well as its transparency, is vitally important to the proper functioning of the eye. If either the surface smoothness or the clarity of the cornea suffers, vision will be disrupted. (Morry1999, Rita2016)

2.2.2.1Corneal Layers

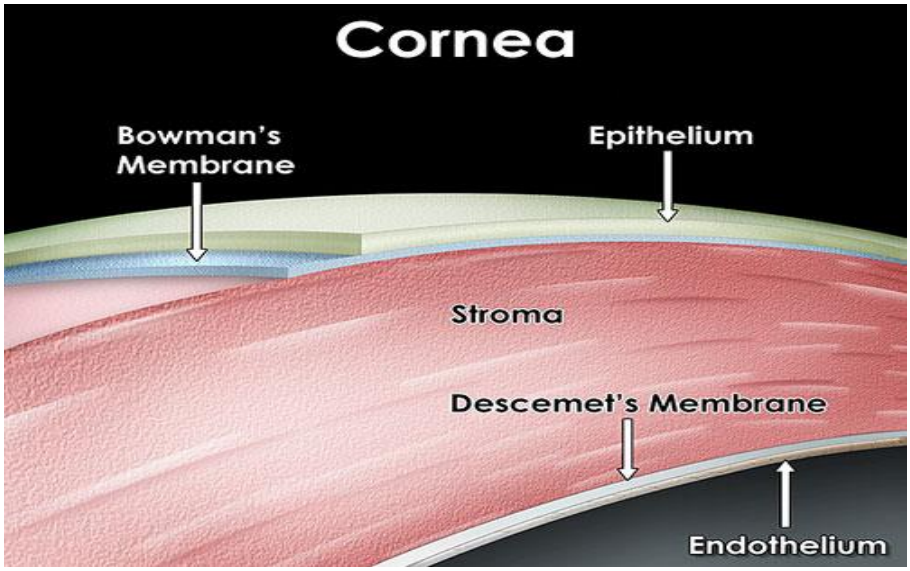

Fig2.7: A cross-section of the Cornea showing distinct layers.

(www.nKcf.org)

Although appearing to be one clear membrane, the cornea is composed of five distinct layers of tissue, each with its own function.

- **Epithelium** is the thin outermost layer of fast-growing and easily-regenerated cells.
- **Bowman's layer** consists of irregularly-arranged collagen fibers and protects the corneal stroma. It is 8 to 14 microns thick.
- **Stroma,** the transparent middle and thickest layer of the cornea is made up of regularly-arranged collagen fibers and keratocytes (specialized cells that secrete the collagen and proteoglycans needed to maintain the clarity and curvature of the cornea)

- **Descemet's membrane** is a thin layer that serves as the modified basement membrane of the corneal endothelium.
- **Endothelium** is a single layer of cells responsible for maintaining proper fluid balance between the aqueous and corneal stromal compartments keeping the cornea transparent. (Morry1999, Rita2016)

2. 2.3 Effect of pregnancy on eyes

Pregnancy can have important effects on the normal physiology and pathophysiology of the mother's eye just as it affects other non-reproductive systems of the mother's body. Knowledge of the ocular changes that occur in association with pregnancy can help in the diagnosis and management of ocular disease in the pregnant woman. (Morry1999, Rita2016)

2.2.3.1 Eyelids

Skin changes are a frequent and polymorphous feature of pregnancy. Chloasma is a blotchy brown discoloration that may occur around the eyelids and usually fades postpartum. Hormonal factors may play a role, either elevated levels of melanocyte stimulating hormone or estrogen and progesterone. Spider angiomas are common during pregnancy and can occur on the eyelids, perhaps related to high estrogen levels. Ptosis has been reported during and following normal pregnancies, with one patient worsening after each of three pregnancies.(Morry1999, Rita2016)

2.2.3.2 Conjunctiva

Changes in conjunctival blood vessels have been described toward the end of normal pregnancies. conjunctival capillaries. The conjunctival epithelium has been shown to undergo cytological changes during pregnancy related to elevated estrogen levels. Vomiting during pregnancy can cause eyelid petechial and subconjunctival hemorrhages. An increase in conjunctival pigmentation can be associated with normal pregnancy. (Morry1999, Rita2016)

2.2.3.3 Cornea

Corneal sensitivity has been found to be decreased in most pregnant women tested, although one study found no change in corneal sensitivity. The sensitivity returns to normal by 2 months postpartum. The corneal sensitivity change does not appear to be related to the amount of increase of corneal thickness or weight gain. (Morry1999, Rita2016)

Corneal thickness has been reported to increase during pregnancy with resolution a short time after delivery in three studies. The amount of increase found varied from 1 micron to 16 microns. The change appears to be present throughout pregnancy The corneal curvature has been found to increase (steepen) by one diopter on average in the second half of pregnancy, with resolution postpartum or after cessation of breastfeeding.(Morry1999, Rita2016)

2.2.3.4 Intraocular Pressure

Studies have found about a 20% decrease in intraocular pressure during pregnancy. This ocular hypotensive effect seems to increase until delivery and may persist for several months postpartum. A greater reduction of intraocular pressure was noted among pregnant women with baseline ocular hypertension in one study. Another investigation showed that the reduction in intraocular pressure was greater among multigravida than prim gravida women. (Morry1999, Rita2016)

2.2.3.5 Lens

The curvature of the crystalline lens has been reported to be increased during pregnancy. A transient loss of accommodation has been reported during and after pregnancy. However, a more recent study failed to demonstrate any change in accommodative amplitude during pregnancy. An increase in lens auto fluorescence has been reported in pregnant patients with diabetes compared

with non-pregnant diabetic patients. This observation suggests the possibility of lenticular metabolic alterations during pregnancy.(Morry1999, Rita2016)

2.2.3.6 Extraocular Muscles

Patients can present with strabismus during pregnancy. A search for pre-existing underlying conditions may help to clarify the diagnosis. For example, three otherwise healthy pregnant women developed a superior oblique palsy during pregnancy. On evaluation, they had amblyopia and decreased stereopsis, suggesting that there may have been decompensation of a latent vertical deviation. One healthy patient developed a transient sixth nerve palsy during pregnancy, unassociated with other changes. (Morry1999, Rita2016)

2.3 Ocular Pathology:

2.3.1 Artery Occlusion

A retinal artery occlusion occurs when the central retinal artery or one of the arteries that branch off of it becomes blocked. This blockage is typically caused by a tiny embolus (clot) in the blood stream. The occlusion decreases the oxygen supply to the area of the retina nourished by the affected artery, causing permanent vision loss (Adler AI et al.2000) In this photograph, the affected area of the retina is the pale, whitish-yellow region (blue arrows) that is normally supplied by the blocked artery (white arrow). The surrounding reddish-orange area is healthy retina tissue. (Deepali Jain, Nat Pernick 2004-2016)

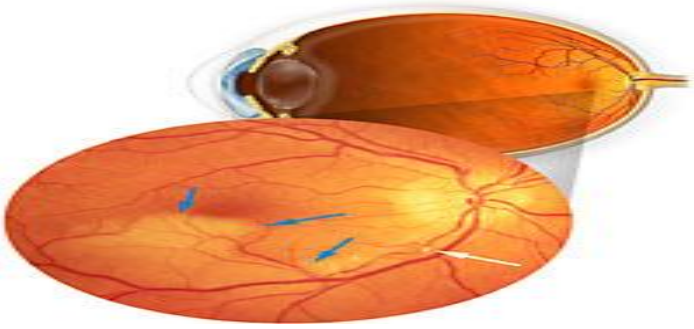

Fig2.8: Artery Occlusion.

(www.mrcmd.com)

2.3.2 Astigmatism

Astigmatism means that the cornea is oval like a football instead of spherical like a basketball. Most astigmatic corneas have a steeper curve and a flatter curve. This causes light to focus on more than one point in the eye, resulting in blurred vision at distance or near. Astigmatism often occurs along with or farsightedness. (Deepali Jain, Nat Pernick 2004-2016)

2.3.3 Basal Cell Carcinoma

Basal cell carcinoma is a type of skin cancer that occurs most commonly on the face or neck, often near an eyelid or on the nose. The tumor cells are thought to originate from the basal, or deepest lasyer of skin. (Trakatelli M et al.2014)

Basal cell carcinoma is the most common type of skin cancer in the United States. Fair-skinned people over age 50 are most commonly affected; it is rare among those with dark skin. The incidence increases significantly with sun exposure. Those who work outdoors or live in sunny climates or areas with high sun exposure are at greater risk. (Trakatelli M et al. 2014)\

The ultraviolet radiation in sunlight is believed to be the cause in most cases. People with dark complexions have more melanin in their skin and are able to

absorb higher amounts of the damaging ultraviolet rays. Since those with fair skin have less melanin, they are less able to withstand the effects of UV exposure. (Trakatelli M et al.2014)

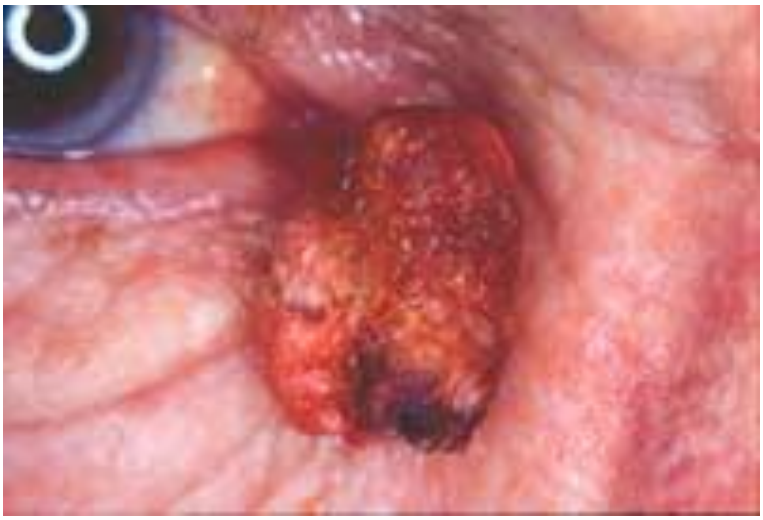

Fig2.9: Basal cell carcinoma.

(www.mrcmd.com)

2.3.4 Blepharitis

Blepharitis is a common inflammatory condition that affects the eyelid. It usually causes burning, itching and irritation of the lids. In severe cases, it may also cause styes, irritation and inflammation of the cornea (keratitis) and conjunctiva (conjunctivitis). Some patients have no symptoms at all.(Deepali Jain, Nat Pernick 2004-2016).

Blepharitis is usually a chronic problem that can be controlled with extra attention to lid hygiene. However, it is sometimes caused by an infection and may require medication. (Deepali Jain, Nat Pernick 2004-2016)

2.3.5 Blowout Fracture

This patient was involved in a car accident where the safety air bag deployed in his face, resulting in a blowout fracture of the bones surrounding his eye. This condition can be painful (especially with eye movement). Eyelid

swelling, restricted eye movement, and nosebleeds are all common signs. Immediate treatment by an ophthalmologist is critical. (Boyette JRet al.2015).

2.3.6 Cataracts

When cataracts are mentioned, people often think of a film that grows on their eyes causing them to see double or blurred images. However, a cataract does not form on the eye, but rather within the eye. (Deepali Jain, Nat Pernick 2004-2016).

A cataract is a clouding of the natural lens, the part of the eye responsible for focusing light and producing clear, sharp images. The lens is contained in a sealed bag or capsule. As old cells die they become trapped within the capsule. Over time, the cells accumulate causing the lens to cloud, making images look blurred or fuzzy. For most people, cataracts are a natural result of aging. (Deepali Jain, Nat Pernick 2004-2016).

In fact, they are the leading cause of visual loss among adults 55 and older. Eye injuries, certain medications, and diseases such as diabetes and alcoholism have also been known to cause cataracts.

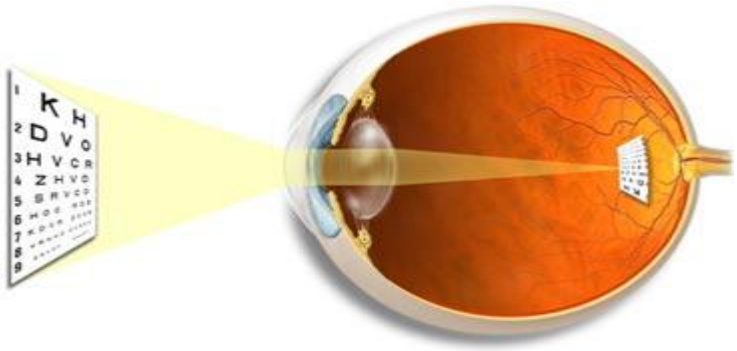

fig2.10:Normal Vision

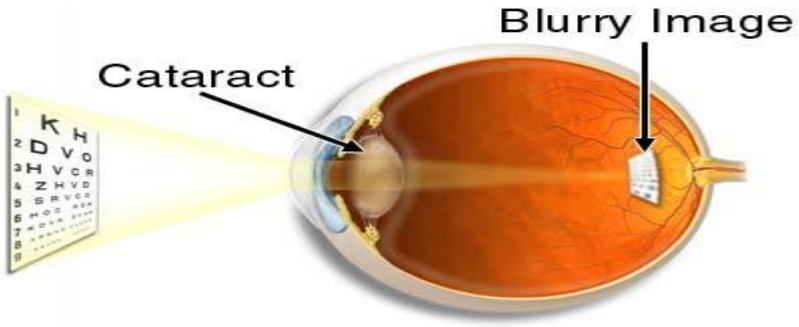

fig2.11:Vision through a Cataract.

(www.roshdypharmacies.com)

2.3.7 Retinal Detachment

Retinal tears commonly occur when there is traction on the retina by the vitreous inside the eye. In a child's eye, the vitreous has an egg-white consistency and is firmly attached to certain areas of the retina. Over time, the vitreous gradually becomes thinner, more liquid and separates from the retina. This is known as a posterior vitreous detachment (PVD). (Fraser et al.2010)

PVDs are typically harmless and cause floaters in the eye; but in some cases, the traction on the retina may create a tear. Retinal tears frequently lead to detachments as fluids seep underneath the retina, causing it to separate and detach. (Fraser et al.2010).

A retinal detachment occurs when the retina's sensory and pigment layers separate. Because it can cause devastating damage to the vision if left untreated,

retinal detachment is considered an ocular emergency that requires immediate medical attention and surgery. It is a problem that occurs most frequently in the middle-aged and elderly. (Fraser et al.2010).

There are three types of retinal detachments. The most common type occurs when there is a break in the sensory layer of the retina, and fluid seeps underneath, causing the layers of the retina to separate. Those who are very nearsighted, have undergone eye surgery, or have experienced a serious eye injury are at greater risk for this type of detachment. Nearsighted people are more susceptible because their eyes are longer than average from front to back, causing the retina to be thinner and more fragile. (Fraser et al.2010).

The second most common type occurs when strands of vitreous or scar tissue create traction on the retina, pulling it loose. Patients with diabetes are more likely to experience this type. (Fraser et al.2010).

The third type happens when fluid collects underneath the layers of the retina, causing it to separate from the back wall of the eye. This type usually occurs in conjunction with another disease affecting the eye that causes swelling or bleeding. (Fraser et al.2010).

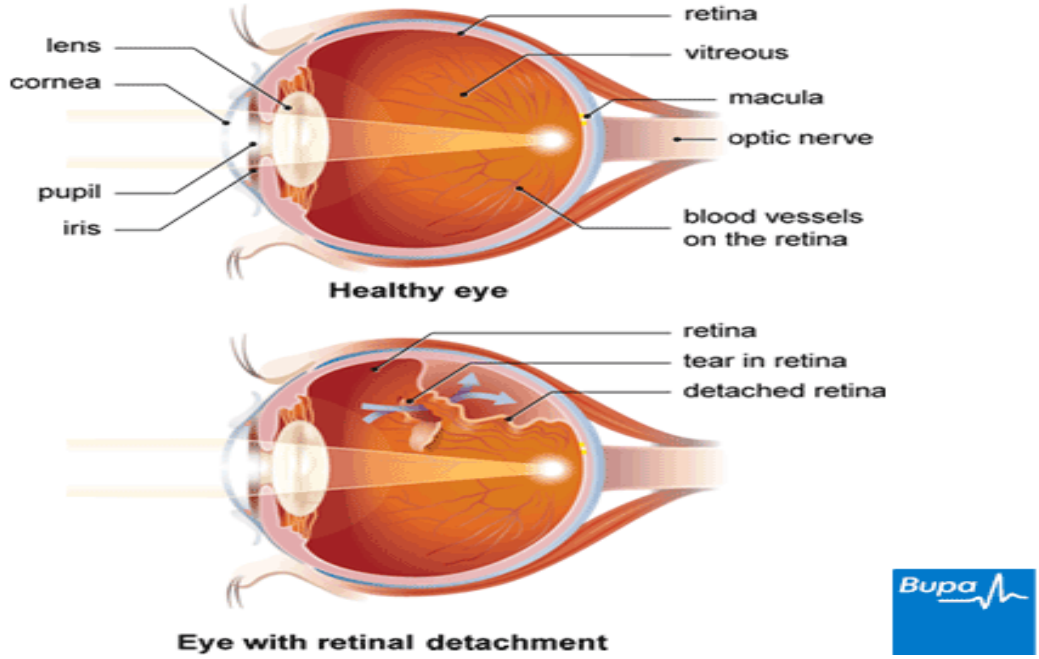

fig2.12:eye with retinal detachment.

(www.roshdypharmacies.com)

2.3.8 Iritis

Iritis is an inflammatory problem of the iris, the colored part of the eye. It often occurs for unknown reasons, but it may be linked to certain diseases affecting the body, infections, previous eye surgery, or injury Iritis may affect one or both eyes. It is sometimes a chronic, recurring condition. (Deepali Jain, Nat Pernick 2004-2016).

2.3.9 Corneal Ulcer

A corneal ulcer forms when the surface of the cornea is damaged or compromised. Ulcers may be sterile (no infecting organisms) or infectious. The term infiltrate is also commonly used along with ulcer. Infiltrate refers to an immune response causing an accumulation of cells or fluid in an area of the body where they don't normally belong. (Deepali Jain, Nat Pernick 2004-2016).

Whether or not an ulcer is infectious is an important distinction for the physician to make and determines the course of treatment. Bacterial ulcers tend to be extremely painful and are typically associated with a break in the epithelium, the superficial layer of the cornea. In some cases, the inflammatory response involves the anterior chamber along with the cornea. Certain types of bacteria, such as Pseudomonas, are extremely aggressive and can cause severe damage and even blindness within 24-48 hours if left untreated. (Deepali Jain, Nat Pernick 2004-2016).

Sterile infiltrates on the other hand, cause little if any pain. They are often found near the peripheral edge of the cornea and are not necessarily accompanied by a break in the epithelial layer of the cornea.

There are many causes of corneal ulcers. Contact lens wearers (especially soft) have an increased risk of ulcers if they do not adhere to strict regimens for the cleaning, handling, and disinfection of their lenses and cases. Soft contact lenses are designed to have very high water content and can easily absorb bacteria and infecting organisms if not cared for properly. Pseudomonas is a common cause of corneal ulcer seen in those who wear contacts. (Deepali Jain, Nat Pernick 2004-2016).

Bacterial ulcers may be associated with diseases that compromise the corneal surface, creating a window of opportunity for organisms to infect the cornea. Patients with severely dry eyes, difficulty blinking, or are unable to care for themselves, are also at risk. Other causes of ulcers include: herpes simplex viral infections, inflammatory diseases, corneal abrasions or injuries, and other systemic diseases. (Deepali Jain, Nat Pernick 2004-2016).

2.3.10Glaucoma

Glaucoma is a disease caused by increased intraocular pressure (IOP) resulting either from a malformation or malfunction of the eye's drainage

structures. Left untreated, an elevated IOP causes irreversible damage the optic nerve and retinal fibers resulting in a progressive, permanent loss of vision. However, early detection and treatment can slow, or even halt the progression of the disease. (Jain, Nat Pernick 2004-2016).

2.3.10.1 Common types of glaucoma

- **Open Angle**

Open angle (also called chronic open angle or primary open angle) is the most common type of glaucoma. With this type, even though the anterior structures of the eye appear normal, aqueous fluid builds within the anterior chamber, causing the IOP to become elevated. Left untreated, this may result in permanent damage of the optic nerve and retina. Eye drops are generally prescribed to lower the eye pressure. In some cases, surgery is performed if the IOP cannot be adequately controlled with medical therapy.(Deepali Jain, Nat Pernick 2004-2016).

- **Acute Angle Closure**

Only about 10% of the population with glaucoma has this type. Acute angle closure occurs because of an abnormality of the structures in the front of the eye. In most of these cases, the space between the iris and cornea is more narrow than normal, leaving a smaller channel for the aqueous to pass through. If the flow of aqueous becomes completely blocked, the IOP rises sharply, causing a sudden angle closure attack.(Deepali Jain, Nat Pernick 2004-2016).

While patients with open angle glaucoma don typically have symptoms, those with angle closure glaucoma may experience severe eye pain accompanied by nausea, blurred vision, rainbows around lights, and a red eye. This problem is an emergency and should be treated by an ophthalmologist immediately. If left untreated, severe and permanent loss of vision will occur in a matter of days. (Deepali Jain, Nat Pernick 2004-2016).

- **Secondary Glaucoma**

This type occurs as a result of another disease or problem within the eye such as: inflammation, trauma, previous surgery, diabetes, tumor, and certain medications. For this type, both the glaucoma and the underlying problem must be treated.(Deepali Jain, Nat Pernick 2004-2016).

- **Congenital**

This is a rare type of glaucoma that is generally seen in infants. In most cases, surgery is required.

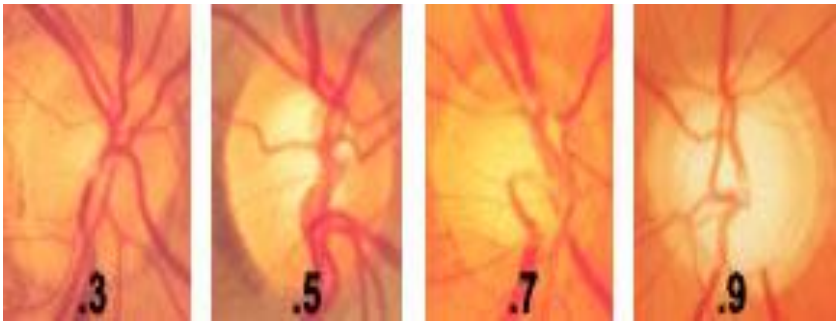

Fig2.13: The above photos show progressive optic nerve damage (indicated by the cup to disc ratio) caused by glaucoma

(www.mrcmd.com)

2.4 Over View Of Diabetes

2.4.1. Definition of Diabetes

Diabetes mellitus is chronic metabolic disorder characterized by tendency to hyperglycemia and to development of atherosclerosis, retinopathy, neuropathy and nephropathy and it is a major factor for coronary heart disease.

2.4.2 Types of Diabetes

There are three main types of diabetes:

Type 1 diabetes: results from the pancreatic failure to produce insulin, and persistency requires insulin replacement. usually begins in childhood; however, it can occur in adults aged 30-40 years. Symptoms of type 1 diabetes may come on quickly.

The eye problem in this type of diabetes occurs in 75% to 95% of adults who have had diabetes for more than 15 years. Diabetic retinopathy in type 1 diabetes is extremely rare before puberty no matter how long they have had the disease. Medical conditions such as good control of sugars, management of hypertension and regulation of blood lipids are important to prevent retinopathy. Fortunately, the vision loss isn't significant in most people with the condition. .(Risérus U.et al.2009)

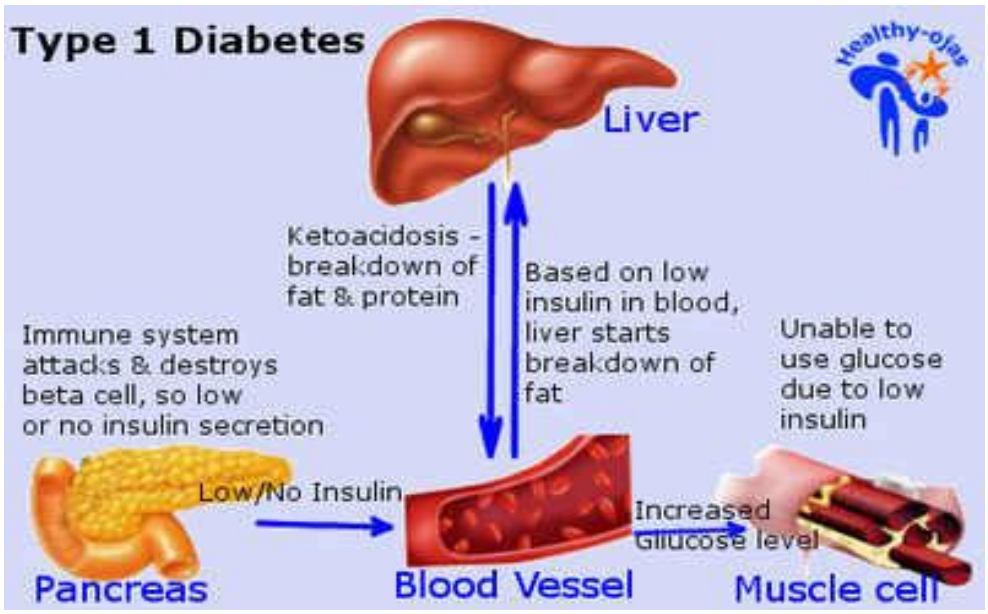

Fig2.14:type 1 diabetes.

(www.alps-europa.eu)

Type 2 diabetes: results from insulin resistance, a condition in which cells fail to use insulin properly, rarely requires treatment with insulin.

Gestational diabetes: when pregnant women, who have never had diabetes before, have a high blood glucose level during pregnancy. It may precede development of type 2 DM.

2.4.3 Causes of Diabetes

Hyperglycemia in all cases is due to a functional deficiency of insulin action. Deficiency in insulin action can be due to decrease in insulin secretion by B cell of the pancreas, or decreased response to insulin by target tissue.

- Other causes of diabetes mellitus include:
- Congenital genetic defects of insulin secretion.
- Cystic fibrosis with pancreatic dysfunction.
- High doses of glucocorticoids steroids.

The cause of diabetes depends on the type. Type1 diabetes is partly inherited and then triggered by certain infections, with some evidence pointing at Coxsackie B4 virus. There is a genetic element in individual susceptibility to some of these triggers which has been traced to particular HLA genotypes. However, even in those who have inherited the susceptibility, type 1 diabetes mellitus seems to require an environmental trigger. Type 2 diabetes is due primarily to lifestyle factors and genetics.(Risérus U.et al.2009)

Following is a comprehensive list of other causes of diabetes: (Mitchell et al.2011)

- Genetic defects of β-cell function.
- Genetic defects in insulin processing or insulin action, e. g: Defects in proinsulin conversion, Insulin gene mutations Insulin receptor, mutations.

- Exocrine Pancreatic Defects, e g: Chronic pancreatitis , Pancreatectomy Pancreatic neoplasia, Cystic fibrosis ,Hemochromatosis.
- Fibrocalculous pancreatopathy Endocrinopathies , e g: Acromemally, Cushing syndrome, Hyperthyroidism, Pheochromocytoma, Glucagonoma.
- Infections, e g: Cytomegalovirus, coxsackievirus B.
- Drugs, e g: Glucocorticoids, Thyroid hormone.

2.4.4 Significant Symptoms of Diabetes

The classical symptoms of DM are polyuria, polydepsia and polyphagia (Cooke DW et al.2008). which may develop rapidly in type 1 diabetes while they are more slowly and may be subtle or absent in T2DM.

Prolonged high blood glucose leads to changes in the retina and lenses of the eyes. Retinal pericytes and microvascular endothelial cells are lost at a very early stage of diabetes. Thickening of the retinal basement membrane is another early change in Diabetic Retinopathy. Death of retinal pericytes and microvascular cells and impairment of basement membrane function are associated with retinal capillary microaneurysm formation and increased vascular permeability .The initial stage of cell death and increased capillary permeability may be followed by cycles of renewal and further cell death, leading to progressive microvascular obliteration, and ischemic retinal injury , hard exudates , new vessels formation in the retina, and macular edema , resulting in vision changes and blindness. .(Risérus U.et al.2009)

People (usually with type 1 diabetes) may also present with diabetic ketoacidosis, a state of metabolic deregulations characterized by the smell of acetone; a rapid, deep breathing known as Kussmaul breathing; nausea; vomiting and abdominal pain; and altered states of consciousness.

A rarer but equally severe possibility is hyperosmolar non ketotic state, which is more common in type 2 diabetes and is mainly the result of dehydration. A number of skin rashes can occur in diabetes that is collectively known as diabetic dermatosis. (Risérus U.et al.2009)

2.4.5 Diagnosis of Diabetes

Diabetes mellitus is characterized by recurrent or persistent hyperglycemia, and is diagnosed by demonstrating any one of the following: Fasting plasma glucose level ≥ 7.0 mmol/L (126 m Posterior ciliary arteries g/dL). Plasma glucose ≥ 11.1 mmol/L (200 mg/dL) two hours after a 75 g oral glucose load as in a test. Symptoms of hyperglycemia and casual plasma glucose ≥ 11.1 mmol/L (200 mg/dL). Glycated hemoglobin (Hb A1C) ≥ 6.5%.

According to the current definition, two fasting glucose measurements above 126 mg/dL (7.0 mmol/L) is considered diagnostic for diabetes mellitus. People with fasting glucose levels from 100 to 125 mg/dL (5.6 to 6.9 mmol /L) are considered to have impaired fasting glucose. Patients with plasma glucose at or above 140 mg/dL (7.8 mmol/L), but not over 200 mg/dL (11.1 mmol/L), 2 hours after a 75 g oral glucose load are considered to have, and both conditions are now labeled as pre diabetic. .(Risérus U.et al.2009)

2.4.6 Management of Diabetes

Management concentrates on keeping blood sugar levels as close to normal as possible by use of dietary advice, exercise, and appropriate medication, Patient education, understanding, and participation to avoid the complications of diabetes which are far less common and less severe in people who have well-managed blood sugar levels.(Nathan DM et al.2005) The goal of treatment is an HbA1C level less than 7%. In addition associated higher risks factors for. (Adler AI et al.2000).

2.4.7 Medications

Metformin is generally recommended as a first line treatment for type 2 diabetes as there is good evidence that it decreases mortality.(Ripsin, CM et al.2009) while type1 diabetes is typically treated with combinations of regular and NPH insulin, or synthetic insulin analogs. When insulin is used in type 2 diabetes, a long-acting formulation is usually added initially, while continuing oral medications. Doses of insulin are then increased to effect.

2.4.8 Complications of Diabetes

2.4.8.1 Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) is an acute medical emergency and dangerous complication that is due to Low insulin levels .the liver shift to fat metabolism by ketosis; ketone bodies are generated as intermediate substrates here. This is normal when periodic, but can become a serious problem if sustained. Elevated levels of ketone bodies in the blood decrease its pH, leading to DKA. The patient in DKA is typically dehydrated, has rapid, deep breathing. Abdominal pain is common and may be severe. The patient is typically conscious until late, when lethargy may progress to coma. Ketoacidosis can easily become severe enough to cause hypotension, shock, and death. Urine analysis will reveal significant levels of ketonuria. Prompt, proper treatment usually results in full recovery, though death can occur due to inadequate or delayed treatment, or brain edema. DKA is more common in type 1 diabetes. (Adler AI et al.2000).

2.4.8.2 Hyperglycemia Hyperosmolar State

Hyperosmolar nonketotic state (HNS) is an acute complication sharing many symptoms with DKA, but an entirely different origin and different treatment. A patient with very high (usually above 300 mg/dl (16 mmol/L)) blood glucose levels has high osmotic effect that cause water to be drawn out

of cells into the blood and the kidneys eventually begin to pass glucose into the urine. This results in loss of water and further increase in blood osmolarity. If fluid is not replaced (by mouth or intravenously), this osmotic effect, combined with water loss, will eventually lead to dehydration. The cells become progressively dehydrated. Electrolyte imbalances are also common and are always dangerous. As with DKA, urgent medical treatment is necessary, commonly beginning with fluid volume replacement. Lethargy may ultimately progress to a coma, though this is seen in type 2 diabetes. (Adler AI et al.2000).

2.4.8.3 Hypoglycemia

It is an acute complication of several diabetes treatments. Otherwise, is rare in diabetic or non-diabetic. Several factors can cause it, such as too much or incorrectly timed insulin dose, too much or incorrectly timed exercise or not enough food. The patient may become agitated, sweaty, weak, and have symptoms of activation of sympathetic autonomic nervous system. Altered Consciousness or even coma can occur in extreme cases, seizures, brain damage and death. The variety of interactions makes cause identification difficult in many cases; iatrogenic hypoglycemia is typically the result of the interplay of absolute (or relative) insulin excess and compromised glucose counter regulation in type 1 and advanced T2DM. Decrements in insulin, increments in glucagon, and increments in epinephrine are the primary glucose counter regulatory factors that normally prevent or correct hypoglycemia. In insulin-deficient diabetes (exogenous) insulin levels do not decrease as glucose levels fall, and the combination of deficient glucagon and epinephrine responses causes defective glucose counter regulation. (Adler AI et al.2000).

Furthermore, reduced sympathoadrenal responses can cause hypoglycemia unawareness. Recent incident of hypoglycemia causes both defective glucose counter regulation and hypoglycemia unawareness. In many cases, short-term

avoidance of hypoglycemia reverses hypoglycemia unawareness in affected patients, although this is not easy in clinical experience.

In most cases, hypoglycemia is treated with sugary drinks or food. In severe cases, an injection of glucagon (induce liver glycogenolysis) or an intravenous infusion of dextrose is used for treatment, but usually only if the patient is unconscious. In hospitals, intravenous dextrose is often used.

2.4.8.4 Diabetic Coma

Diabetic coma is a medical emergency in which diabetic patient is comatose due to acute complications of diabetes like: Severe hypoglycemia, severe DKA due to combination of severe hyperglycemia, dehydration and shock, and exhaustion. Or Hyperosmolar nonketotic coma in which extreme hyperglycemia and dehydration are sufficient to cause coma. (Adler AI et al.2000).

2.4.8.5 Respiratory infections

The immune response is impaired in diabetic patient. Many factors lead to an increase susceptibility to respiratory infections such as pneumonia and influenza among diabetic patients. With associated worse prognosis and slower recovery.

2.4.9 Complications of Chronic Hyperglycemia

Chronic hyperglycemia leads to damage of blood vessels. The vascular endothelial cells take in more glucose than normal, since they do not depend on insulin. They then form more surface glycoprotein's which cause basement membrane thickening and weakness. This damage to small blood vessels leads to microangiopathic, which can cause one or more of Diabetic cardiomyopathy, leading to diastolic dysfunction and eventually heart failure. (Adler AI et al.2000).

2.4.9.1 Diabetic Nephropathy

Diabetic nephropathy, damage to the kidney which can lead to chronic renal failure. Diabetic nephropathy is the most common cause of adult renal failure worldwide in the developed world.

2.4.9.2 Diabetic Neuropathy

Abnormal and decreased sensation, usually in a "glove and stocking" distribution starting with the feet, later often fingers and hands. When combined with damaged blood vessels this can lead to diabetic foot. Other forms of diabetic neuropathy may present as mononeuritis or autonomic neuropathy, Diabetic amyotrophy. (Adler AI et al.2000).

2.2.9.3 Diabetic Retinopathy

Growth of friable and poor-quality new blood vessels in the retina as well as macular edema, which can lead to severe vision loss or blindness. Retinal damage makes it common cause of blindness. (Adler AI et al.2000)

2.4.9.4 Macrovascular Disease

Leads to cardiovascular disease, to which accelerated atherosclerosis is a contributor; CAD, leading to angina or myocardial infarction , Diabetic myonecrosis ,stroke, Peripheral vascular disease, which contributes to intermittent claudication as well as diabetic foot. The latter is often due to a combination of sensory neuropathy and vascular damage. Can be complicated by infection, necrosis and gangrene. (Adler AI et al.2000).

2.4.9.5 Diabetic Encephalopathy

Diabetic encephalopathy is the increased cognitive decline and risk of dementia observed in diabetes. Including alterations to the vascular supply of

the brain and the interaction of insulin with the brain itself. (Adler AI et al.2000).

2.4.10 Diabetes mellitus and pregnancy:

Until recently, getting pregnant was a risky business for a diabetic woman, and even riskier for her unborn baby. Today, with expert medical care and guidance and scrupulous self-care, the diabetic woman has just about as good a chance of having a successful pregnancy and healthy baby as any other pregnant woman does. The commoner type of situation is, however where you are diagnosed in pregnancy to have abnormal sugars. (Dr. R. L. Bhatia et al.2005)

Making your diabetic pregnancy a success will take a good deal of effort on your part, but the reward – a healthy baby – will make it well worth the effort. Research has proved that the key to successfully managing diabetic pregnancy is maintaining euglycemia (normal blood sugar levels).(Dr. R. L. Bhatia et al.2005)

2.4.10.1 Carbohydrate Metabolism During Pregnancy

Pregnancy uncovers the diabetic tendencies of symptomatic women. This is due to the progressive increase in insulin resistance that occurs during pregnancy. There is an antagonism to the action of insulin – (the key hormone, which maintains blood sugar levels) because of the new hormonal environment of pregnancy. (Dr. R. L. Bhatia et al.2005)

2.4.10.2 Effect of pregnancy on Diabetes

These patients (women) have high tendencies towards (metabolic) complications and need frequent glucose monitoring, strict treatment protocols and highly regulated life style. Women with a tendency towards Non-Insulin

dependent Diabetes Mellitus may show high blood sugars for the first time, during pregnancy. (Dr. R. L. Bhatia et al.2005).

2.4.10.3 Effect of Diabetes on pregnancy

These women have a greater incidence of complications like pre-eclampsia (high blood pressure during pregnancy) infection, post-delivery bleeding (PPH) and caesarean deliveries. The fetuses have high incidence of congenital anomalies, hypoglycemia (low levels of glucose), macrosomia (big size baby > 4.5kg), breathing problems, low levels of calcium (hypocalcemia) and traumatic deliveries. (Dr. R. L. Bhatia et al.2005).

2.5.1 Smoking and eye disease

Tobacco smoke is composed of at least 7000 active chemicals, most of them toxic and potentially damaging to the eye.(U.S.D.S.et al.2010) Smoking can cause or worsen several eye disorders, in particular Age-related Macular Degeneration (AMD), which may lead to blindness.

fig 2.15:Image show effect of smoking on eye
(www.doingyoudamage.com)

2.5.2 How smoking affects sight

Ongoing exposure to tobacco smoke generates biological changes in the eye that can lead to vision loss. Heavy exposure to secondhand smoke, such as living with a smoker for at least five years, can also cause these changes.(Khan JC et al.2006)The chemicals in tobacco smoke reduce the body's ability to protect itself by concurrently increasing the levels of oxidants and decreasing the levels of antioxidants in the body. (U.S.D.S.et al.2010)

High blood pressure, directly caused by smoking, is a risk factor for macular degeneration. Smoking causes blood vessels to narrow throughout the body, including the blood vessels to the eye.(U.S.D.S.et al.2010) Smoking also reduces the amount of oxygen in the blood so less oxygen reaches the macula.(N.H)

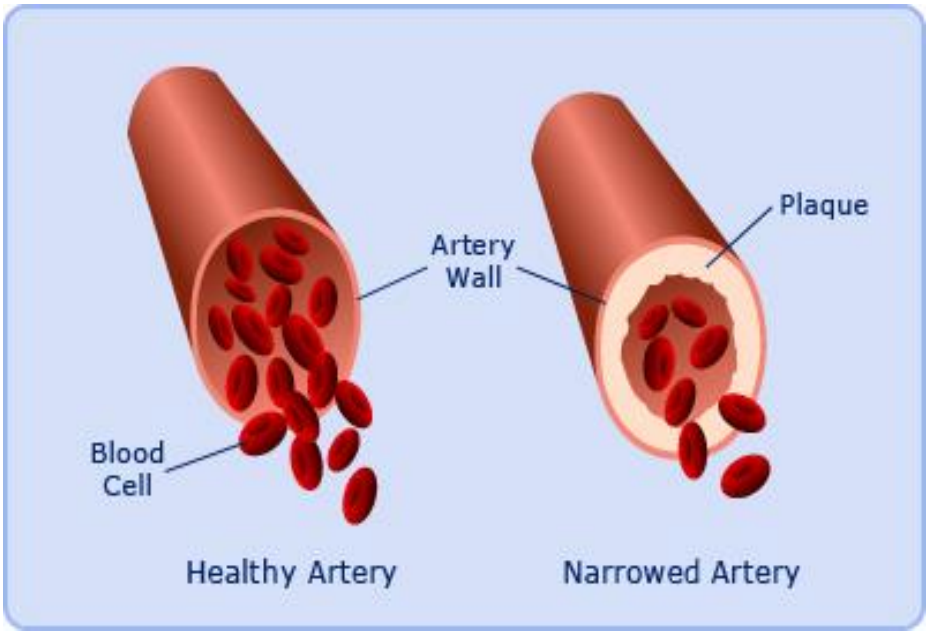

fig 2.16:Effect of smoking in blood vessels
(www.fhmnanobor.com)

2.5.3 Some Major Ocular Diseases Due To Smoking

- Chronic Irritable eye
- Cataract
- Age related macular degeneration

- Retinal Vascular disorders
- Tobacco amblyopia
- Ischemic optic Neuropathy
- Thyroid eye disease
- Malignancy
- Open angle Glaucoma
- Diabetic Retinopathy
- Ocular Sarcoidosis
- Miscellaneous - Nystagmus, Strabismus, Retinal Detachment, Leber's Optic Neuropathy.

2.5.3.1 Chronic irritable eye

The conjunctival mucosa is highly sensitive to airborne chemicals, fumes and irritative gases that originate in tobacco smoke in active and passive smoking.(Gometto-Muniz JE et al.1992) Excessive lacrimation, stinging, burning, pricking sensations are common symptoms and conjunctival congestion with metaplastic changes in mucosa may be seen.

A study on the influence of exposure to environmental tobacco smoke (ETS) in an aircraft, on measured and perceived cabin air quality, nasal patency and biomarkers in nasal lavage fluid was conducted by(Weislander et al.2000). He concluded that despite a high air exchange rate and spatial separation between smokers and non-smokers, smoking in commercial aircraft may cause significant air pollution, as indicated by large increase in the number of respirable particles. This ETS exposure is associated with an increase in ocular and general symptoms, decreased tear film stability and alterations of nasal patency.

2.5.3.2 Cataracts

A cataract is a clouding in the lens of the eye that causes blurred vision and, if left untreated, can lead to vision loss.(A.C.H.S et al.2003) Cataracts often develop as part of the normal ageing process.

Smoking is a major risk factor in the development of cataracts.(Verity DH et al.2013) Compared with never smokers, smokers of 20or more cigarettes per day are at least twice as likely to develop a nuclear cataract. (Verity DH et al.2013) A smoker's risk of developing cataracts increases with the amount smoked; cataracts are more severe in heavy smokers than in light smokers. (Verity DH et al.2013)

Antioxidants help maintain lens transparency. Although the exact mechanism by which smoking causes cataracts to develop is not fully understood, the destruction of antioxidant nutrients by tobacco smoke is a plausible hypothesis. (Bedinghaus Tet al.2013) Cigarette smoking may also break down other micronutrients critical to healthy eye tissues. .(A.C.H.S et al.2003)

2.5.3.3 Age-related macular degeneration (AMD)

Age related macular degeneration (AMD) is an umbrella term for a variety of degenerative changes in the macula, the small central area of the retina at the back of the eye which is responsible for clear, central vision(U.S.D.S.et al.2010).When the macula is affected, vision becomes blurred, distorted and dark in the center (this is called a scotoma). (A.C.H.S et al.2003) Although peripheral vision is not affected by AMD, loss of central vision means that everyday activities such as reading, driving and watching television, cannot be performed. .(A.C.H.S et al.2003)

Smoking is the major preventable risk factor for AMD (both wet and dry forms). (Zhang X1 et al.2011) Smoking at least doubles or triples the risk of developing AMD, which tends to develop earlier in smokers.(R.C.O.2013) As mentioned above, there is a dose-response relationship with the number of pack-years of smoking. (U.S.D.S.et al.2010).

Smoking causes oxidative stress and damages the retina, reduces blood flow in eye tissue, and promotes ischaemia, hypoxia, and micro-infarctions. (U.S.D.S.et

al.2010).It also causes cell death to retinal pigment epithelium cells, likely(Cano M et al 2010) through one of the toxic chemicals present in tobacco smoke, benzo(e)pyrene, as was found in an in vitro study. (Sharma A et al.2008).Smokers are more likely to suffer from all types of AMD and more likely to develop the disease ten years earlier than non-smokers. (Sharma A et al.2008).

The risk of developing AMD is also greater for smokers with a genetic predisposition. (R.C.O.2013). The interaction between genetics and smoking is also a factor to be considered.(Barnett BP et al.2013)Since scientists are just beginning to determine who is at greatest risk, based on their genetic makeup and smoking status, the best way to avoid this additional risk is to not smoke. (R.C.O.2013)

2.5.3.4 Retinal Vascular Disorders

Smoking is considered a major risk factor in most ischemic disorders, affecting the ocular vasculature at various levels. Both erythrocyte and leucocyte levels are elevated in smokers, and platelets are activated in the blood of long-term smokers. These factors contribute to hyperviscosity and an increased risk of thrombosis. Nicotine, a principal ingredient of tobacco smoke, causes stimulation of adrenergic vascular receptors, leading to vasoconstriction. The increased carbon monoxide concentration in blood that results from cigarette smoking decreases the oxygen carrying capacity of haemoglobin. These factors further contribute to smoking induced ischemic and hypoxic environment of the tissues. (Benowitz NL1986) Amaurosis fugax, a transient episode of monocular visual loss, is commonly seen in smokers. Tobacco smoke accelerates the rate of atherosclerosis and retinal emboli, composed of cholesterol or platelet fibrin aggregate are responsible for these transient ischemic spells or even retinal infarction. (Tippin J et al.1989)Smoking is also a risk factor for retinal artery occlusion. (Wong DF et al.2000)

According to a study by Klein R et al in 2000, Retinal vein occlusion was strongly associated with smokers as compared to non-smokers (odds ratio 4.43,95% confidence interval 1.53, 12.84), apart from other risk factors.(Klien R et al.2000)

2.5.3.5 Tobacco amblyopia

This is an important cause of bilateral optic neuropathy and is characterized by a distinct bilateral severe visual disturbance, symmetrical scotomas and color vision defects. According to (Mojon D et al.2001), smoking interrupts mitochondria function and ocular tissues with high energy consumption and dependence on oxidative energy production, like optic nerve and retina are often involved in mitochondria diseases like optic neuropathy, retinal degeneration, decreased ocular motility and unilateral ptosis. Optic nerve has been found to be more vulnerable to tobacco smoke than peripheral nerves. (H.FukushimaK et al.1989)

Cyanide detoxification incapacity and deficiency of Vitamin B12 are possible causes of tobacco amblyopia. (Jestico JV et al.1984) have reported raised whole blood cyanide levels in patients with tobacco amblyopia (approaching lethal levels reported from acute cyanide inhalation). This is due to the impaired cyanide detoxification in cigarette smokers.

An interesting new neuro-ophthalmological sign was reported by Kellen R et al -He described a yellow forelock in a in a middle aged man with loss of vision in both eyes(Rizzo JF et al.1993) reported 2 cases of tobacco amblyopia out of which one recovered with cessation of smoking, indicating the beneficial role of avoiding tobacco in this condition.

2.5.3.6 Optic neuropathy

Anterior ischaemic optic neuropathy (AION) is an eye disease that results in a sudden, painless loss of vision, often leading to permanent blindness. It occurs because of reduced blood flow in the arteries to the eyes. (Bedinghaus T.2013) .Atherosclerosis – clogging of the arteries – may be responsible for AION. Smokers are at a 16-fold increased risk of developing AION compared with nonsmokers. (Bedinghaus T.2013) Furthermore, smokers develop optic neuropathy at younger ages: in one study smokers were found to develop the disease at an average age of 52 and non-smokers at an average age of 6

2.5.3.7 Thyroid eye disease (TED)

Cessation of smoking is an important local measure in the treatment of thyroid eye disease according to(Comblatt et al,2000) apart from achievement of a euthyroid state, artificial tears and assessment for development of optic neuropathy, proptosis, diplopia and lid abnormalities.Tobacco ingredients competitively inhibit iodine uptake and organification in the gland. The influence of smoking on the sympathetic nervous system also affects thyroid function. The hypoxia induced by vasoconstriction due to nicotine, stimulates protein synthesis and extra-ocular muscle derived fibroblast proliferation leading to hypertrophy & Graves ophthalmopathy.

2.5.3.8 Malignancy

Ocular metastasis in carcinomas related to smoking (e.g. lung carcinoma) have been reported by Hasturk et al. (Bertelsen JB et al.1994) A patient with basaloid large cell lung carcinoma presented concurrently with a metastatic uveal tumor, leading to retinal detachment. Small cell carcinoma of the lung may present with ptosis and Homers syndrome if apex of the lung is involved.

2.5.3.9 Diabetic retinopathy

Diabetic retinopathy is an eye complication associated with diabetes in which the blood vessels that supply the retina are damaged by high blood sugar levels. (Bedinghaus.T.2013)When these blood vessels become damaged, they may leak fluid or blood and grow scar tissue which can distort the images the retina sends to the brain. (Cai J et al.2002)This can eventually lead to blindness. (RNIB et al.2013)

Smoking is a significant risk factor for developing diabetic retinopathy. In one (Hammes HP et al.2011)Brazilian study, smoking more than doubled and almost tripled the risk of developing advanced diabetic retinopathy.(Esteves JF et al.2009)Smoking may accelerate the development of this condition or, as shown in some studies, worsen it, because smoking damages blood vessels.(Zhong ZLet al.2011)

A possible mechanism leading to damage of the retina is smoking-induced hypoxia. (Klein R et al.2010). This condition is a result of diminished oxygen in the blood, with a corresponding increase in carbon monoxide.(Mulhauser I.et al.1996)Smoking also increases blood pressure and raises blood sugar levels in diabetics, therefore making it harder to controzal the diabetes.

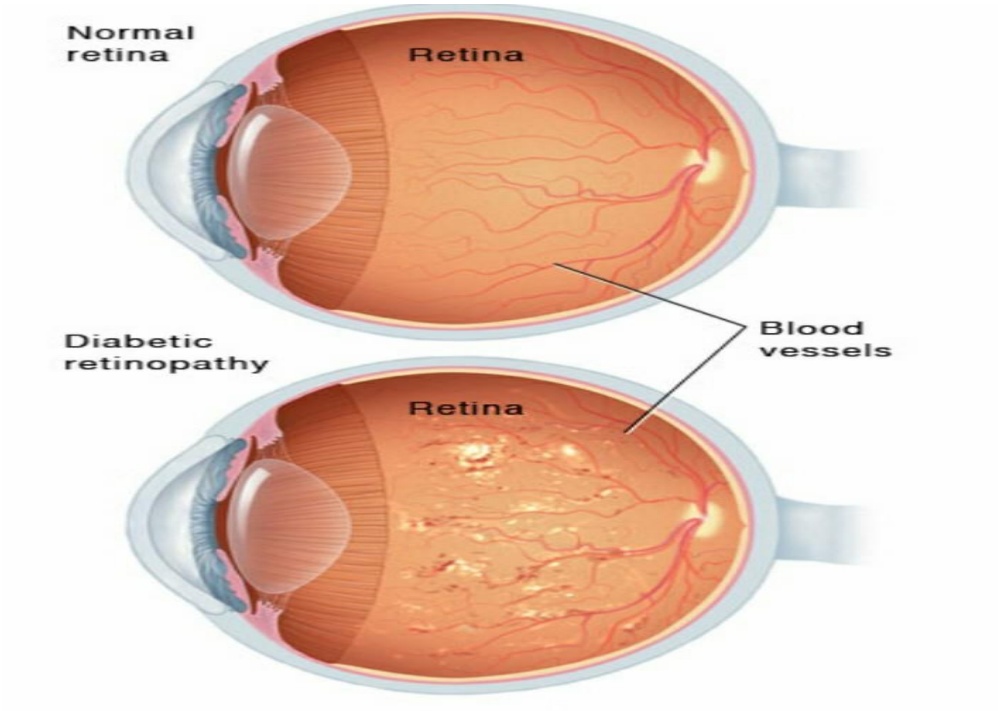

Fig2.17: Comparison between normal eye and eye with diabetic retinopathy (www.rebuildyourvision.com)

2.5.3.10 Ocular Sarcoidosis

Tobacco dust is known to contain non-biodegradable foreign bodies. Incomplete phagocytosis of these particles evokes an antigenic response in the immunologically susceptible host .Therefore smoke may be an important environmental risk factor for ocular sarcoidosis as was investigated by(Merritt JC et al.1986)

2.6.1Ultrasound

Sound is a physical phenomenon that transfers energy from one point to another. One of the most significant characteristics of sound is its frequency, which is the rate at which the sound source and the material vibrate. The basic unit for specifying frequency is the hertz, which is one vibration, or cycle, per second. Pitch is a term commonly used as a synonym for frequency of sound. (Perry Sprawls,http://www.sprawls.org/resources)

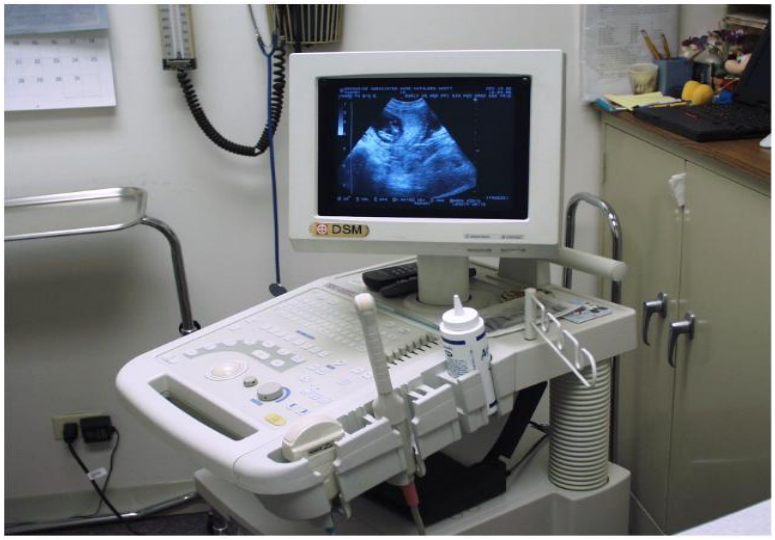

Fig. 2.18: Modern Ultrasound Machine.
(www.ultrasound.com**)**

The human ear cannot hear or respond to all sound frequencies. The range of frequencies that can be heard by a normal young adult is from approximately 20 Hz to 20,000 Hz (20 kHz). Ultrasound has a frequency above this range. Frequencies in the range of 2 MHz (million cycles per second) to 20 MHz are used in diagnostic ultrasound. Ultrasound is used as a diagnostic tool because it can be focused into small, well-defined beams that can probe the human body and interact with the tissue structures to form images (Figures: 2.1 & 2.2). (Perry Sprawls, http://www.sprawls.org/resources)

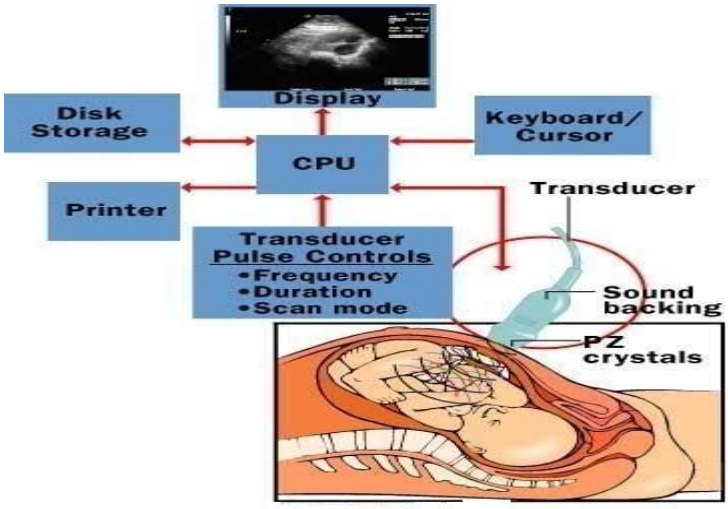

Fig. 2.19: ultrasound imaging procedure.

(www.physics.utoronto.ca)

2.6.2Ultrasound Machine

The transducer is the component of the ultrasound imaging equipment that is placed in direct contact with the patient's body. It performs several functions as will be described in detail later. It's first function is to produce the ultrasound pulses when electrical pulses are applied to it. A short time later, when echo pulses return to the body surface they are picked up by the transducer and converted back into electrical pulses that are then processed by the system and formed into an image. (Perry Sprawls, http://www.sprawls.org/resources)

When a beam of ultrasound pulses is passed into a body, several things happen. Most of the ultrasound energy is absorbed and the beam is attenuated. This is undesirable and does not contribute to the formation of an image like in x-ray imaging. Some of the pulses will be reflected by internal body structures and send echoes back to the surface where they are collected by the transducer and used to form the image. Therefore, the general ultrasound image is a display of structures or reflecting surfaces in the body that produce echoes as illustrated below. (Perry Sprawls, http://www.sprawls.org/resources)

2.6.3 The Basic Ultrasound Imaging Process

Echoes, which show up as bright or white spots in the image is produced by surfaces or boundaries between two different types of tissues. Most anatomical areas are composed of a "mixture" of different tissue types and many surfaces that produce the general gray and white background that we see in the image. Since there are no reflecting surfaces within a fluid, such as a cyst, it is dark in the image. Therefore, the general ultrasound image, sometimes called a "B mode" image, is a display of echo producing sites within the anatomical area. (Perry Sprawls, http://www.sprawls.org/resources)

The ultrasound image is a display showing the location of reflecting structures or echo sites within the body. The location of a reflecting structure (interface) in the horizontal direction is determined by the position of the beam. In the depth direction, it is determined by the time required for the pulse to travel to the reflecting site and for the echo pulse to return. (Perry Sprawls, http://www.sprawls.org/resources)

Another physical characteristic that can be imaged with ultrasound is motion, specifically the motion of flowing blood. This uses the Doppler principle and the images are usually displayed with different colors representing the different flow velocities and directions.

2.6.4 The ultrasound imaging system

The basic functional ultrasound components of an imaging system are shown below.

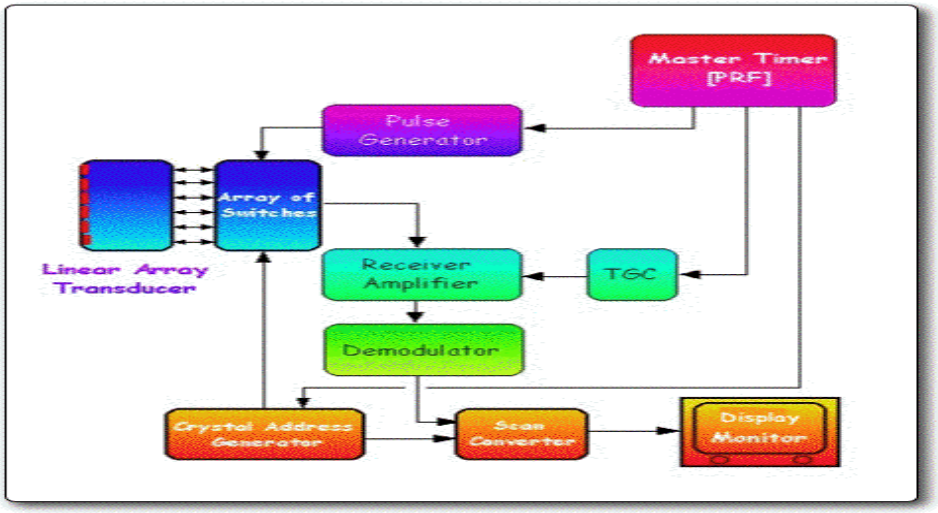

Fig. 2.20:Ultrasound imaging system
(en.wikibooks.org)

2.6.4.1 Transducer

The transducer is the component of the ultrasound system that is placed in direct contact with the patient's body. It alternates between two major functions: (1) producing ultrasound pulses and (2) receiving or detecting the returning echoes. (Perry Sprawls, http://www.sprawls.org/resources)

2.6.4.2 Pulse generators

The pulse generator produces the electrical pulses that are applied to the transducer.

2.6.4.3 Amplification

Amplification is used to increase the size of the electrical pulses coming from the transducer after an echo is received.

2.6.4.4 Scan Generator

The scan generator controls the scanning of the ultrasound beam over the body section being imaged. This is usually done by controlling the sequence in which the electrical pulses are applied to the piezoelectric elements within the transducer. (Perry Sprawls, http://www.sprawls.org/resources)

2.6.4.5 Scan converter

Scan conversion is the function that converts from the format of the scanning ultrasound beam into a digital image matrix format for processing and display.

2.6.4.6 Image processor

The digital image is processed to produce the desired characteristics for display. This includes giving it specific contrast characteristics and reformatting the image if necessary. (Perry Sprawls, http://www.sprawls.org/resources)

2.6.4.7 Display

The digital ultrasound images are viewed on the equipment display (monitor).

2.6.2Eye and Orbit Ultrasound

An eye and orbit ultrasound uses high-frequency sound waves to measure and produce detailed images of your eye and eye orbit. The orbit is the socket in your skull that holds your eye. This test provides a much more detailed view of the inside of your eye than is possible during a routine eye exam. (Ann Pietrangelo et al.2015)

Sometimes called eye studies, an ultrasound technician or an ophthalmologist usually performs the procedure. Eye studies can be done in an office, outpatient imaging center, or hospital. Your eye doctor may order eye studies if you're experiencing unexplained problems with your eyes or if you've recently sustained an injury or trauma to the eye area.

This procedure is helpful in identifying issues with the eyes and diagnosing eye diseases. For example, some issues the test can help identify include:

- tumors or neoplasms involving the eye
- foreign substances
- detachment of the retina

An eye and orbit ultrasound can also be used to help diagnose or monitor:

- glaucoma (a progressive disease that can lead to vision loss)
- cataracts (cloudy areas in the lens)
- lens implants (plastic lenses implanted in the eye after the natural lens has been removed, usually due to cataracts)

Doctors can also use this procedure to measure the thickness and extent of a cancerous tumor and determine treatment options. (Ann Pietrangelo et al.2015)

2.6.3. Procedure and Preparation

- **Preparation**

An eye and orbit ultrasound requires no specific preparation. No pain is associated with an eye and orbit ultrasound. Anesthetic drops will be used to numb your eye and minimize discomfort. Your eyes will not be dilated. (Ann Pietrangelo et al.2015)

Vision may be temporarily blurred during the test. Patients should be able to drive a half hour after the procedure, but may feel more comfortable arranging for someone else to drive. Your eye doctor will advise you not to rub your eyes after the procedure until the anesthetic has completely worn off. This is so you don't scratch your cornea. (Ann Pietrangelo et al.2015).

- **Procedure**

There are two parts to an eye and orbit ultrasound. The A-scan ultrasound takes measurements of the eye. The B-scan allows the doctor to see clearly into the back of the eye. The combined procedure (A and B scans) will take 15 to 30 minutes to complete. (Ann Pietrangelo et al.2015)

- **A-Scan**

The A-scan measures the eye. This is useful in determining the correct lens implant for cataract surgery. While sitting upright in a chair, you'll place your chin on a chin rest and look straight ahead. A probe that has been oiled will be placed against the front portion of your eye as it's scanned.An A-scan can also be performed while you're lying down. In that case, a fluid-filled cup, or water bath, is placed against the surface of your eye as it's scanned. (Heikkilä, K et al.2011*)*

- **B-Scan**

The B-scan helps your doctor see the space behind the eye. Cataracts and other conditions make it difficult to see the back of the eye. The B-scan also helps in the diagnosis of tumors, retinal detachment, and other conditions. (1 During a B-scan, you'll be in a seated position with your eyes closed. Your eye doctor will put a gel on your eyelids. They'll tell you to keep your eyes closed while moving them in many directions. Your eye doctor will place the probe against your eyelids.*(* Heikkilä, K et al.2011*)*

2.6.4 Risks of Eye and Orbit Ultrasound

This is a quick and painless procedure with no serious side effects or risks. *(* Heikkilä, K et al.2011)

2.7.1Doppler Ultrasonography

2.7.1.1Definition

Doppler ultrasonography is a non-invasive diagnostic procedure that changes sound waves into an image that can be viewed on a monitor. (Heikkilä, K et al.2011)

2.7.1.2Types of Doppler ultrasound

The four basic types of Doppler ultrasound are:

- Bedside" or continuous wave Doppler.
- Duplex Doppler.
- Color Doppler
- Power Doppler

2.7.1.3 Purpose

Doppler ultrasonography can detect the direction, velocity, and turbulence of blood flow. It is frequently used to detect problems with heart valves or to measure blood flow through the arteries. Specifically, it is useful in the work up of stroke patients, in assessing blood flow in the abdomen or legs, and in viewing the heart to monitor carotid artery diseases. (Heikkilä, K et al.2011)

2.7.1.4 Precautions

The test is widely used because it is noninvasive, uses no x rays, and gives excellent images. It is harmless, painless, and widely available.

2.7.1.5 Description

Doppler ultrasonography makes use of two different principles. The ultrasound principle is this: when a high-frequency sound is produced and aimed at a target, it will be reflected by its target and the reflected sound can be detected back at its origin. In addition, it is known that certain crystals (called piezoelectric crystals) produce an electrical pulse when vibrated by a returning sound. The Doppler principle is simply that sound pitch increases as the source moves toward the listener and decreases as it moves away.(Heikkilä, K et al.2011)

Medical science utilizes these two principles in the following way. A transducer (sometimes called a probe) containing piezoelectric crystals sends a series of short sound pulses into the body and pauses between each pulse to listen for the returning sounds. The machine then determines the direction and depth of each returning sound and coverts this into a point of light on a television monitor. Thousands of these pulses are computed and displayed every second to produce an image of the organ being studied. The image allows the doctor to see the organ functioning in real time. (Morry1999, Rita2016)The newest addition to

this test is the addition of color. Adding color to the image shows the direction and rate of blood flow more clearly. (Heikkilä, K et al.2011)

A Doppler ultrasonography procedure the technician will apply a gel to the skin, then place the transducer against the skin at various angles. The transducer sends the information it receives to a television monitor that shows a moving image of the organ being studied. The technician can save these images either on video tape, paper, or x-ray film for further study. (Heikkilä, K et al.2011)

2.7.1.6 Preparation

There is no special preparation needed for this test. The ultrasound technician may apply a clear gel to the skin in order to help the transducer more freely over the body. (Heikkilä, K et al.2011)

2.7.1.7Aftercare

No aftercare is necessary.

2.8.1Color Doppler Imaging (CDI)

CDI is an established method for investigation of the ocular and orbital blood flow characteristics. It is an ultrasonographic method that has been employed for the evaluation of the circulatory status in much ocular pathology, but is most used for the investigation of the circulatory status in retinal vascular disorders and in glaucoma.(MacKinnon JR et al.2000)

Ultrasound imaging (sonography) is accomplished with a pulse-echo technique. Pulses of ultrasound (generated by a transducer) are sent into the patient where they produce echoes at organ boundaries and within tissues. These echoes then return to the transducer, they are being detected and then displayed.

Color-flow imaging extends the use of the pulse-echo imaging principle. Echoes returning from stationary tissues are detected and presented in greyscale in

appropriate locations along the scan line. The depth is determined by the echo's arrival time and the brightness is determined by the echo's amplitude. If a returning echo has a different frequency than what is emitted a frequency change has occurred because the echo-generating object was moving. If the motion is towards or away from the transducer, the Doppler shift is positive or negative, respectively. Along with the transducer, the color-flow instrument consists of a pulser, a beam-former, a receiver, a memory and a display .

In ophthalmology, CDI is most often used to study the circulatory parameters in the retro bulbar blood vessels – the central retinal artery, central retinal vein, ophthalmic artery and the short and long posterior ciliary arteries. However, intraocular blood vessels have also been studied, such as vortex veins, blood vessels in the intraocular tumours, in detached retina, etc. The measurement is usually obtained through closed eyelids in a supine or in a seated position. Nagahara et al. patented a device for CDI measurement in seated subjects that increased the reproducibility of the measurement by 50% .(Nagahara M et al.2002)

The reflected ultrasound from the moving cells in the measured blood vessels is recorded by the CDI device and represented as a velocity wave.

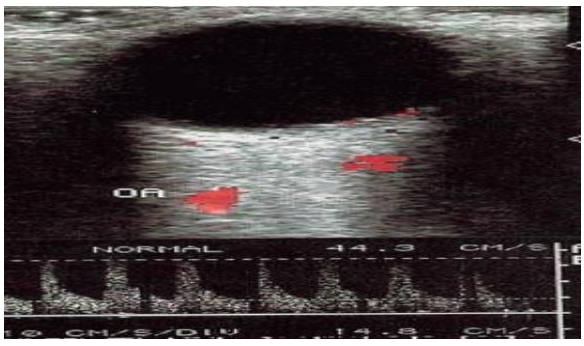

Fig2.21:Normal Color Doppler image and waveform on an OA

(www.entokey.com)

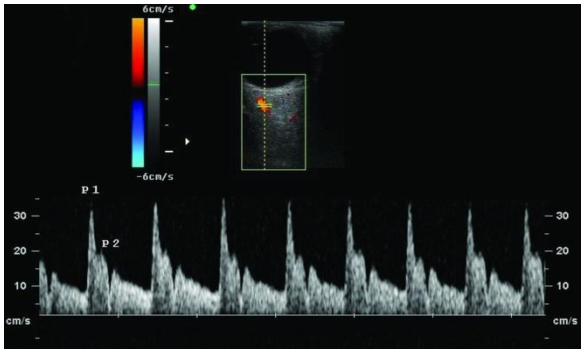

Fig2.22: Doppler velocimetry of the ophthalmic artery in a normal pregnant woman (www.jultrasoundmed.org)

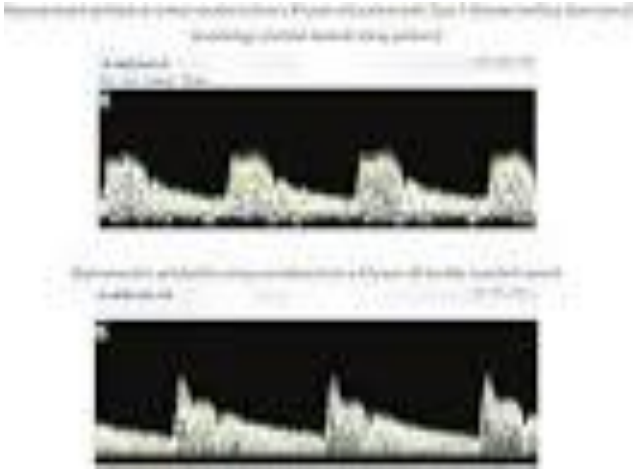

Fig 2.23:Ophthalmic artery wave in patient with type 1 diabetes

(Openi.nlm.nih.gov)

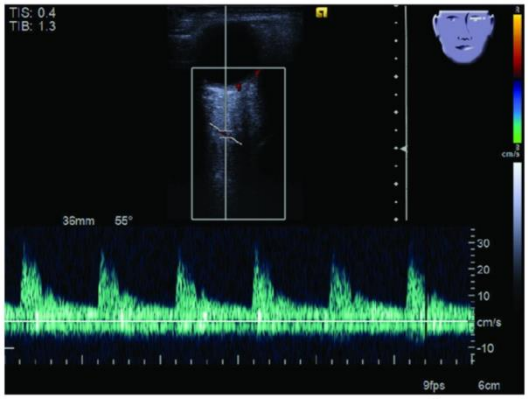

Fig 2.24:Normal Color Doppler image and waveform on an OA

(www.researchgate.net)

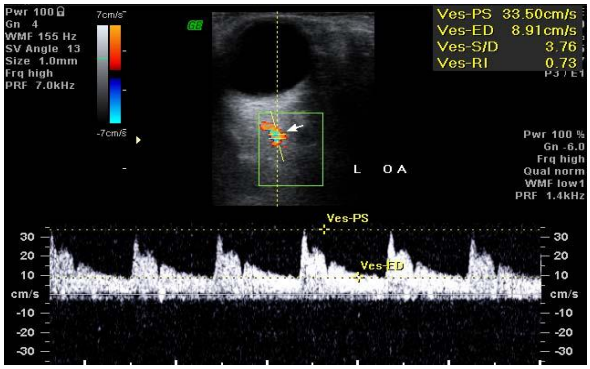

fig 2.25:Ophthalmic artery blood flow velocity in the Diabetic group showed a decrease in peak systolic velocity and RI was increased.

(www.jcdr.net)

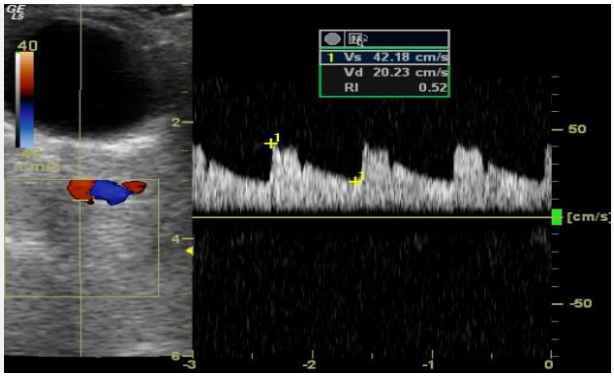

Fig 2.26: Assessment of ophthalmic artery resistance index with patient lying supine with eyes closed and using an ultrasound frequency of 7.5 mHz. The transducer is applied to the closed upper eyelid using a thick layer of acoustic gel, minimizing pressure on the globe.

(Openi.nlm.nih.gov)

Fig 2.27: AO Doppler showing the typical wave of a patient with RDP

(www.webcir.org)

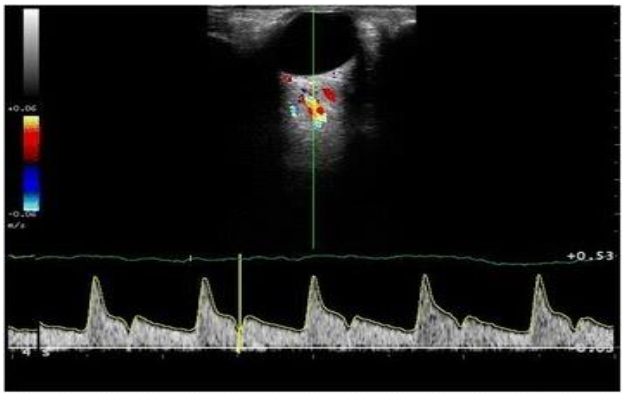

Fig 2.28:Doppler ultrasound of right ophthalmic artery.

(Openi.nlm.nih.gov)

2.9.1 Previous studies

Maria Marta et al (2013), compared the ophthalmic artery (OA) perfusion of pregnant smokers and nonsmokers by Doppler indexes. Correlate these with the interval of last cigarette, cigarettes per day, years smoking and carbon monoxide expired (COex). The Transversal study involving 70 pregnant smokers divided into 33 pregnant who smoked until 2 h: A group (AG) and B group (BG): 37, who smoked between 2 and 24 h before test. Control group (CG) was composed of 51 pregnant nonsmokers. Doppler indexes were assessed: PSV (Peak Systolic Velocity), EDV (End Diastolic Velocity), PI (Pulsatility Index), RI (Resistance Index) and PR (Peak Ratio). Groups were compared using ANOVA, Kruskal–Wallis test, Student's t test, Mann–Whitney and Pearson's correlation coefficient, whereas $p < 0.05$. RI and PI were higher ($p < 0.01$) and PSV and EDV were lower ($p < 0.05$) in B group compared to other groups. A group presented higher PR ($p < 0.01$) compared to control. AG presented years of smoking, cigarettes per day, COex greater than BG and lower interval of last cigarette than BG. On the basis of results of present study, it was concluded that OA in pregnant smokers shows a biphasic pattern of perfusion correlated with the time of consumption of the last cigarette. There were signs of vasoconstriction and hypoperfusion to tobacco

exposure between 2 and 24 and hyperperfusion in A Group compared to B Group.

Gil Hernández et al (2004) studied the differences of blood flow in type I diabetes patients using a color Doppler ultrasound they measured the systolic peak velocity (Vmax), diastolic velocity (Vmin) as well as the resistance index in the central retinal artery (CRA) and in the ophthalmic artery (OA) using a color Doppler ultrasound in 40 diabetic patients. they classified the patients according to the duration of diabetes, which ranged from 1 to 28 years. and whether retinopathy was present. they compared the results against those obtained in the 40 control subjects without vascular pathology, When the results of the two groups were compared, they found that no decrease was observed in the CRA flow rate in diabetics without retinopathy, however there was a significant decrease in flow velocity in patients with initial ($p<0.05$), moderate ($p<0.001$) or proliferative retinopathy ($p<0.05$). The ophthalmic artery presents an increase in the vascular resistance in diabetics with proliferative retinopathy. As the time of diabetes increases, there is a decrease in the blood flow in CRA and an increase in resistance in the OA.

Takashi Arai.et al (1998) investigate ocular blood flow hemodynamics in patients with diabetes mellitus. They used color Doppler sonography, in 22 normal subjects and 52 patients with ($n = 25$) or without ($n = 27$) diabetic retinopathy, to determine blood flow velocities and the resistive index of the central retinal artery. The resistive index of the central retinal artery in patients with diabetic retinopathy (0.85 ± 0.09) was significantly greater ($P < 0.01$) than that in normal subjects (0.72 ± 0.08) and in patients without diabetic retinopathy (0.81 ± 0.09). The resistive index of the central retinal artery in the patients without diabetic retinopathy was also significantly greater than that of normal subjects ($P < 0.01$). The resistive index of ocular arterial flow was increased in the patients with diabetes mellitus and further increased in the presence of retinopathy. Increased resistance in the peripheral ocular vascular bed

contributes to diabetic retinopathy, and this change is present before the appearance of overt diabetic retinopathy.

Steigerwalt.et al(2000) investigate ocular and orbital blood flow in cigarette smokers. The color duplex scanner was used to measure the systolic and diastolic flow velocity of the OA, CRA, and PCA in 10 smokers and 11 non smokers. Both the systolic and diastolic flow velocity decreased in the OA, CRA, and PCA in smokers compared with nonsmokers. The systolic flow decreased by as much as 36% and the diastolic flow by as much as 52%. This decrease was significant for the flow velocity of the CRA and PCA but not for the OA, An increase in the resistance index was also found.

The authors believe that the decrease in the flow velocity of these vessels may be due to an increase in the vascular resistance of the vessels of the retina and optic nerve head in smokers. This may be important in patients with eye disease in whom altered blood flow already contributes to the ocular or orbital pathology.

Toshiyuki Hata1, et al, evaluate whether maternal ophthalmic artery pulsatility index (PI) in normotensive pregnancies with type 1 diabetes is different from that in normal normotensive pregnancies. The ophthalmic artery in 15 normal normotensive pregnant women, and 13 normotensive pregnant women with type 1 diabetes was studied once with colour Doppler flow imaging and pulsed Doppler ultrasonography after 16 weeks gestation. The heart rate, mean arterial blood pressure, and ophthalmic artery PI were calculated in each group. The PI (1.94 ± 0.45) in normotensive pregnant women with type 1 diabetes was significantly lower than that (2.73 ± 0.32) in normal normotensive pregnant women ($P < 0.0001$). There was no significant difference in maternal heart rate or mean arterial blood pressure between the two groups. These results suggest that vascular resistance in the maternal orbital circulation is reduced in pregnancies with type 1 diabetes that are normotensive. The lower

PI in pregnant women with type 1 diabetes should be interpreted as orbital vascular vasodilatation, indicating orbital hyperperfusion or hyperaemia.

Paes MM[1] et al(2013),compare the ophthalmic artery (OA) perfusion of pregnant smokers and nonsmokers by Doppler indexes. Correlate these with the interval of last cigarette, cigarettes per day, years smoking and carbon monoxide expired (COex).Transversal study involving 70 pregnant smokers divided into 33 pregnant who smoked until 2 h: A group (AG) and B group (BG): 37, who smoked between 2 and 24 h before test. Control group (CG) was composed of 51 pregnant nonsmokers. Doppler indexes were assessed: PSV (Peak Systolic Velocity), EDV (End Diastolic Velocity), PI (Pulsatility Index), RI (Resistance Index) and PR (Peak Ratio). Groups were compared using ANOVA, Kruskal-Wallis test, Student's t test, Mann-Whitney and Pearson's correlation coefficient, whereas $p < 0.05$.RI and PI were higher ($p < 0.01$) and PSV and EDV were lower ($p < 0.05$) in B group compared to other groups. A group presented higher PR ($p < 0.01$) compared to control. AG presented years of smoking, cigarettes per day, COex greater than BG and lower interval of last cigarette than BG. The OA in pregnant smokers shows a biphasic pattern of perfusion correlated with the time of consumption of the last cigarette. There are signs of vasoconstriction and hypoperfusion to tobacco exposure between 2 and 24 and hyperperfusion in A Group compared to B Group.

Gil Hernández MA , et al(2001).study the differences of blood flow in type I diabetes patients using a color Doppler ultrasound. We measured the systolic peak velocity (Vmax), diastolic velocity (Vmin) as well as the resistance index in the central retinal artery (CRA) and in the ophthalmic artery (OA) using a color Doppler ultrasound in 40 diabetic patients. We classified the patients according to the duration of diabetes, which ranged from 1 to 28 years. and whether retinopathy was present. We compared the results against those

obtained in the 40 control subjects without vascular pathology .When the results of the two groups were compared, we found that no decrease was observed in the CRA flow rate in diabetics without retinopathy, however there was a significant decrease in flow velocity in patients with initial ($p<0.05$), moderate ($p<0.001$) or proliferative retinopathy ($p<0.05$). The ophthalmic artery presents an increase in the vascular resistance in diabetics with proliferative retinopathy. As the time of diabetes increases, there is a decrease in the blood flow in CRA and an increase in resistance in the OA. The Doppler ultrasound is a non-invasive technique which allows us to perform a hemodynamic study of the orbital vessels. It is essential to understand the correlation between blood flow velocity and the severity of retinopathy in diabetes patients as it manifests the relationship between the velocity of the blood flow with the severity of the retinopathy and that there is a direct relationship with the evolution of the diabetes and the flood flow velocity.

Tamaki Y et al(1993) was used Color Doppler imaging to analyze the blood velocity in the ophthalmic artery (BVA) of 33 normal subjects and 36 diabetic patients. Maximum systolic BVA (Vmax), minimum end-diastolic BVA (Vmin) and Pourcelot index (RI: index of vascular resistance) were determined by analyzing the pulse wave of flow velocity in the ophthalmic artery. The coefficient of reproducibility of Vmax, Vmin and RI in normal subjects was 10%, 9% and 4%, respectively, when analyzed twice at one-hour intervals. There was no significant difference in the indices of the right eyes compared to those of the left eyes. The averages of Vmax, Vmin and RI were 25.4 +/- 7.6 cm/s, 6.3 +/- 2.3 cm/s and 0.75 +/- 0.052 (mean +/- SD), respectively. Vmax and Vmin decreased significantly with age (Vmax: $r = -0.65$, $P < 0.001$; Vmin: $r = -0.61$, $P < 0.001$). RI did not change with age. Vmax, Vmin and RI were compared between normal subjects and patients. RI was significantly higher in diabetics (0.775 +/- 0.047 in patients without retinopathy, 0.779 +/- 0.084 in patients with background retinopathy and 0.786 +/- 0.081 in patients with preproliferative or proliferative retinopathy) than in normal

subjects (0.728 +/- 0.054). This suggests there is a pathological increase in choroidal vascular resistance and/or a decrease in the diameter of the ophthalmic artery in diabetics.

Jane R. MacKinnon, et al (2000) measure blood flow velocity in the ophthalmic artery (OA) and central retinal artery (CRA) in patients with diabetic retinopathy.62 age-matched subjects divided into 3 groups: non-diabetic controls (n=17); diabetics with no clinical retinopathy or background changes (n=24); diabetics with either pre-proliferative or proliferative retinopathy (n=21). Colour Doppler imaging was performed on supine patients by one masked observer using the Acuson 128 machine. There was a statistically significant ($p<0.05$) decrease in both the peak systolic velocity (PSV 0.073 m/s) and end diastolic velocity (EDV 0.014 m/s) of the central retinal artery in the pre-proliferative/proliferative group compared to the no retinopathy/background retinopathy group (PSV 0.096 m/s, EDV 0.024 m/s) and the control group (PSV 0.142 m/s, EDV 0.029 m/s). The resistance index of the ophthalmic artery was significantly increased in both the pre-proliferative/proliferative (0.81) and the no retinopathy/background group (0.81) compared to controls (0.72).Reduced blood flow velocity was found in the CRA of diabetic patients and appeared to become further reduced with the progression of retinopathy. This suggests that monitoring with Colour Doppler imaging may have predictive power in identifying those at greatest risk of developing sight threatening proliferative disease. The resistance index of the OA was increased in diabetics compared to controls.

Chapter Three

Materials &Methods

Chapter Three

Material

3.1.1 Material

Equipment Some of patients were scanned with Voluson E6 and other patients with Medison ultrasound machine.

fig 3. 1:Voluson E6

3.1.2 Examination technique:

Color Doppler U/S, High-frequency transducers(linear array transducer) the scans are usually performed with the patient supine and eye closed. Usually 7.5 MHZ ultrasound scanner have been used and applied with contact jelly through the closed upper lid while examiner's hand rests upon the orbital margin to minimize the pressure on the globe. Horizontal scan through the eye and orbit are performed.

Depending on the direction of flow with respect to transducer, the blood flow data is displayed in either red or blue. All patients was scanned three times in(first, second and third trimester to show the change of ophthalmic artery flow by measuring RI, PI and MV for both eye)

3.2. Method

3.2.1 Study Design

This s study is of descriptive, cross- sectional hospital-based type.

3.2.2 Study Area

The study was conducted in Saudi Arabia at(Al-Amin and Al-Ousrah poly clinic)

3.2.3 Study Period

This Study was conducted during the period from July 2012 - August 2016.

3.2.4 Study Population

Pregnant woman with T1DM who are attending for follow up at Al-Amin and Al-Ousrah poly clinic, in whom the diagnosis of pregnancy and T1DM was made on the basis of clinical history and laboratory criteria. I asked patients about if they are smoker or not.

3.2.5 Study Group

Sample1: was divided into 3groups: group 1 included 15Pregnant Diabetic ladies: their ages were between (30-39) years old,. Group 2 were fourteen healthy pregnant ladies; their ages were between (30-37) years. Group 3 was the Control group and their ages were (30-41) years.

Sample2: was divided into 4 groups: group 1 were normal healthy pregnant ladies (N=57) , group 2 were smokers pregnant ladies (N=44) ,group 3 were diabetic pregnant ladies (N=64),and group 4 were diabetic smoke pregnant ladies (N=71) ladies.

All patients were recruited from Al-Amin and Al-Ousrah poly clinic. The four groups were matching in age, sex and number of individuals to exclude the effect of these parameters on the study outcome.

3.2.5.1 Inclusion Criteria

- pregnant woman whose age from 30-40yrs.
- Those with history of diabetic With pregnancy.
- Those pregnant woman without history of diabetic
- Those pregnant woman with history of smoking.
- Those pregnant woman with history of smoking and diabetes.
- Those with no history of other diabetic complications such as nephropathy, retinopathy, or uncontrolled hypertension.
- Who will agree to participate in this study will be enrolled.

3.2.5.2 Exclusion Criteria

- Patient s age <30 or >40 years.
- Patient with DMT2or Gestation diabetes.
- Patient who already had Eye diseases.
- Those who use any medication.
- Those with current illness (such as hepatic, cardiac or renal disease).

3.3Tools

3.3.1 Consent

Verbal consent was taken from hospital administer, treating doctors & from the patients. No identification or individual details were published. No

information or patient details will be disclosed or used for reasons other than the study.

3.3.2 Data collection

Questionnaire was designed containing data regarding the persona details: name, age, duration of diabetes and their management, Color Doppler and Ultra sound finding of both eyes.

3.3.3Data analysis

Analyzed using SPSS Program .T-test was used to compare means .All values expressed as mean ± SD, and P values of <0.05 were considered to be statistically significant.

Chapter Four

Results

CHAPTER FOUR

RESLUTS

Ultrasound scanning was performed in the Ultrasound Unit of-Al.Amin and Al-Ousrah poly clinic .All patients was scanned three times in first, second and third trimester . RI, PI and MV Correlation is significant at $p \leq 0.05$

Result of Maternal ophthalmic artery Doppler indices in type 1 diabetes during pregnancy:

The sample was divided into 3groups: group 1 included15Pregnant Diabetic ladies: their ages were between (30-39) years old, 8(53.3%) out of 15 were under diet control, 7(46.7%) were insulin dependent, 14(93.3%) used regular insulin treatment where 1(6.7%) uses the insulin in irregular manner. Group 2 were fourteen healthy pregnant ladies; their ages were between (30-37) years. Group 3 was the Control group and their ages were (30-41) years.

Detailed results are shown in the tables below:

Table(4.1): Doppler Indices Left Eye and Right Eye of 15 Pregnant type 1Diabetic ladies.

Doppler Indices Left Eye			
	RI	**PI**	**MV**
First Trimester	0.7±0.3	1.2±0.7	6.5±2.1
Second Trimester	1.4±0.3	3.2±0.7	6.2±1.1
Third Trimester	1.8±0.2	4.5±0.9	4.8±1.2
P-value	0.000*	0.000*	0.009*
Total	1.3±0.5	3.0±1.6	5.8±1.7
Doppler Indices Right Eye			
	RI	**PI**	**MV**
First Trimester	0.7±03	1.4±0.6	0.4±2.8
Second Trimester	1.4±0.3	3.3±0.7	5.8±1.2
Third Trimester	1.6±0.3	4.9±0.4	4.0±1.3
P-value	0.000*	0.000*	0.005*
Total	1.2±0.5	3.2±1.6	5.4±2.1

Values are expressed as Mean ± SD; * Significant at P-value < 0.05.

Table (4. 2): Doppler Indices of Left Eye and Right Eye and treatment as Diet control and Insulin.

Doppler Indices Left Eye			
	RI	**PI**	**MV**
Diet Control	1.5±0.1	3.5±0.5	5.6±0.7
Insulin	1.4±0.2	3.1±0.4	5.8±1.0
P-value	0.157	0.158	0.792
Total	1.4±0.2	3.3±0.5	5.7±0.8
Doppler Indices Right Eye			
	RI	**PI**	**MV**
Diet Control	1.4±0.2	3.6±0.5	5.7±0.4
Insulin	1.3±0.0	3.3±0.0	5.9±0.0
P-value	0.383	0.758	0.201
Total	1.3±0.2	3.6±0.4	5.8±1.1

Values are expressed as Mean ± SD; * Significant at P-value < 0.05.

Table(4. 3): Doppler Indices Left Eye and Right Eye of 14 healthy Pregnant ladies.

Doppler Indices Left Eye			
	RI	**PI**	**MV**
First Trimester	0.5±0.2	0.9±0.5	8.1±2.0
Second Trimester	0.8±0.2	1.7±0.5	6.7±1.4
Third Trimester	0.6±0.2	3.0±0.9	5.7±1.0
P-value	0.002*	0.000*	0.001*
Total	0.7±0.2	1.9±1.1	6.8±1.8
Doppler Indices Right Eye			
	RI	**PI**	**MV**
First Trimester	0.6±02	1.0±0.7	8.1±3.4
Second Trimester	0.9±0.2	1.8±0.8	6.2±1.5
Third Trimester	1.3±0.3	0.9±2.0	5.1±1.5
P-value	0.000*	0.000*	0.006*
Total	0.9±0.4	2.0±1.1	6.5±2.6

Values are expressed as Mean ± SD; * Significant at P-value < 0.05.

Table (4.4): Comparison between the three groups (Control, Pregnanttype1Diabetic & healthy pregnant ladies):

Doppler Indices Eye	Control	Pregnant Diabetic	Pregnant Normal	P-value
Right Eye RI	0.8±0.1	1.3±0.2	1.0±0.2	0.000*
Right Eye PI	1.6±0.4	3.6±0.4	22±0.7	0.000*
Right Eye MV	8.4±3.2	5.2±1.1	6.2±1.3	0.001*
Left Eye RI	0.7±0.1	1.4±0.2	0.9±0.2	0.000*
Left Eye PI	1.6±0.3	3.3±0.5	2.1±0.5	0.000*
Left Eye MV	8.5±3.2	5.7±0.8	6.5±0.7	0.001*

Values are expressed as Mean ± SD; * Significant at P-value < 0.05.

Result of A Study of Maternal Ophthalmic Artery Doppler Indices in Diabetics and Smokers:

The sample was divided into 4 groups: group 1 were normal pregnancy (N=57) , group 2 were pregnant smokers(N=44) ,group 3 were diabetic pregnant ladies (N=64),and group 4 were diabetic smoke pregnant ladies =71 ladies. Pregnant ladies were assessed and traced during the pregnancy period as once in first, second and third trimester for OA Doppler indices for both right and left eyes.

Table(4.5) : Descriptive statistics of the measured values (RI), (PI), (MV) in all of the studied groups in first , second and third trimester.

Studied groups	Site	N	Resistivity index (RI)*	Mean	Std Deviation	Pulsatility index (PI)*	Mean	Std. Deviation	Mean Velocity (MV)*	Mean	Std. Deviation
Normal Pregnancy	Left Eye	57	RI1	0.63	.26	PI1	1.20	0.540	MVI	7.52	1.79
		57	RI2	1.01	.35	PI2	1.87	0.571	MV2	6.52	1.46
		57	RI3	1.24	.34	PI3	2.28	0.543	MV3	5.18	1.52
	Right Eye	57	RI1	0.70	.26	PI1	1.29	0.541	MVI	7.64	1.49
		57	RI2	1.03	.33	PI2	1.91	0.615	MV2	6.18	1.41
		57	RI3	1.26	.35	PI3	2.46	0.539	MV3	4.87	1.74
Smoker Pregnant Ladies	Left Eye	44	RI1	0.80	.31	RI1	1.45	0.33	MVI	8.38	1.61
		44	RI2	1.20	.34	RI2	2.21	0.44	MV2	7.52	1.39
		44	RI3	1.58	.32	RI3	2.84	0.42	MV3	6.69	1.33
	Right Eye	44	RI1	0.85	.38	RI1	1.47	0.30	MVI	8.50	1.53
		44	RI2	1.18	.39	RI2	2.16	0.48	MV2	7.46	1.33
		44	RI3	1.51	.44	RI3	3.47	4.65	MV3	6.68	1.32
Diabetic Pregnant Ladies	Left Eye	64	RI1	0.88	.35	RI1	1.31	.56	MVI	7.12	1.64
		64	RI2	1.45	.39	RI2	2.57	.69	MV2	5.90	1.52
		64	RI3	1.84	.50	RI3	3.38	.47	MV3	4.64	1.56
	Right Eye	64	RI1	0.90	.44	RI1	1.30	.67	MVI	6.89	1.59
		64	RI2	1.43	.42	RI2	2.62	.77	MV2	5.52	1.59
		64	RI3	1.80	.46	RI3	3.34	.59	MV3	4.46	1.68
Smoker Diabetic Pregnant Ladies	Left Eye	71	RI1	0.98	.44	RI1	1.63	.56	MVI	7.43	1.67
		71	RI2	1.35	.40	RI2	2.73	.53	MV2	6.38	1.64
		71	RI3	1.72	.28	RI3	3.74	.59	MV3	5.30	1.62
	Right Eye	71	RI1	1.01	.50	RI1	1.58	.59	MVI	7.80	1.52
		71	RI2	1.43	.38	RI2	2.77	.56	MV2	6.81	1.56
		71	RI3	1.67	.30	RI3	3.74	.68	MV3	5.58	1.48

(RI)stands for Resistivity index, (PI)for pulsatility index, (MV) for Mean Velocity in all of the studied groups in first , second and third trimester(RI1,RI2,RI3 and PI1,PI2,PI3 and MV1,MV2,MV3)

Table(4.6) : Correlations between the measured values for Resistivity index (RI), pulsatility index (PI), MeanVelocity (MV) in all of the studied groups in first , second and third trimester in all pregnancy condition. Correlation is significant at $p \leq 0.05$.

Studied Group	SITE	Resistivity index (RI)*	Correlation	Sig.	Pulsatility index (PI)*	Correlation	Sig.	Mean Velocity (MV)*	Correlation	Sig.
Normal pregnancy	Left Eye	R1&R2	.247	.064	P1&P2	.450	.000	MV1&MV2	.835	.000
		R2&R3	.758	.000	P2&P3	.521	.000	MV2&MV3	.674	.000
	Right Eye	R1&R2	.328	.013	P1&P2	.605	.000	MV1&MV2	.544	.000
		R2&R3	.731	.000	P2&P3	.725	.000	MV2&MV3	.698	.000
Smoker Pregnant Ladies	Left Eye	R1&R2	.246	.107	P1&P2	.226	.141	MV1&MV2	.898	.000
		R2&R3	.373	.013	P2&P3	.302	.046	MV2&MV3	.910	.000
	Right Eye	R1&R2	.497	.001	P1&P2	.589	.000	MV1&MV2	.879	.000
		R2&R3	.445	.002	P2&P3	.097	.531	MV2&MV3	.867	.000
Diabetic Pregnant Ladies	Left Eye	R1&R2	.428	.000	P1&P2	.347	.005	MV1&MV2	.769	.000
		R2&R3	.544	.000	P2&P3	.528	.000	MV2&MV3	.835	.000
	Right Eye	R1&R2	.515	.000	P1&P2	.245	.051	MV1&MV2	.633	.000
		R2&R3	.595	.000	P2&P3	.261	.038	MV2&MV3	.827	.000
Smoker Diabetic Pregnant Ladies	Left Eye	R1&R2	.567	.000	P1&P2	.263	.026	MV1&MV2	.722	.000
		R2&R3	.500	.000	P2&P3	.075	.536	MV2&MV3	.840	.000
	Right Eye	R1&R2	.540	.000	P1&P2	.239	.045	MV1&MV2	.847	.000
		R2&R3	.544	.000	P2&P3	.387	.001	MV2&MV3	.663	.000

(RI)stands for Resistivity index, (PI)for pulsatility index, (MV) for Mean Velocity in all of the studied groups in first , second and third trimester(RI1,RI2,RI3 and PI1,PI2,PI3 and MV1,MV2,MV3)

Table(4.7) : Paired Samples test showed the Paired Differences between the measured values for Resistivity index(RI), pulsatility index (PI), Mean Velocity (MV) in all of the studied groups in first , second and third trimester in all pregnancy conditions .Correlation is significant at p≤0.0

Studied Group	Site	RI	Paired Differences		Sig (2-tailed)	PI	Paired Differences		Sig (2-tailed)	MV	Paired Differences		Sig (2-tailed)
			Mean	STDV			Mean	STDV			Mean	STDV	
Normal Pregnancy	Left Eye	R1-R2	-381	.39	.000	P1-P2	-67	0.58	.000	MV1-MV2	1.00	.98	.000
		R2-R3	-233	.24	.000	P2-P3	-41	0.54	.000	MV2-MV3	1.34	1.20	.000
	Right Eye	R1-R2	-329	.35	.000	P1-P2	-62	0.51	.000	MV1-MV2	1.45	1.39	.000
		R2-R3	-227	.25	.000	P2-P3	-55	0.43	.000	MV2-MV3	1.31	1.26	.000
Smoker Pregnant Ladies	Left Eye	R1-R2	-.404	.40	.000	P1-P2	-.75	0.48	.000	MV1-MV2	0.85	0.71	.000
		R2-R3	-384	.37	.000	P2-P3	-62	0.51	.000	MV2-MV3	0.82	0.58	.000
	Right Eye	R1-R2	-.333	.39	.000	P1-P2	-.68	0.39	.000	MV1-MV2	1.04	0.73	.000
		R2-R3	-.321	.44	.000	P2-P3	-1.3	4.63	0.69	MV2-MV3	0.78	.68	.000
Diabetic Pregnant Ladies	Left Eye	R1-R2	-575	.40	.000	P1-P2	-1.2	0.72	.000	MV1-MV2	1.22	1.08	.000
		R2-R3	-.385	.43	.000	P2-P3	-.81	0.06	.000	MV2-MV3	1.26	.088	.000
	Right Eye	R1-R2	-528	.42	.000	P1-P2	-1.3	0.89	.000	MV1-MV2	1.36	1.36	.000
		R2-R3	-370	.40	.000	P2-P3	-.72	0.84	.000	MV2-MV3	1.05	0.96	.000
Smoker Diabetic	Left Eye	R1-R2	-.368	.39	.000	P1-P2	-1.1	0.66	.000	MV1-MV2	1.05	1.23	.000
		R2-R3	-.370	.35	.000	P2-P3	-1.0	0.77	.000	MV2-MV3	1.08	0.92	.000
Pregnant Ladies	Right Eye	R1-R2	-.426	.43	.000	P1-P2	-1.1	0.71	.000	MV1-MV2	0.98	0.85	.000
		R2-R3	-.238	.33	.000	P2-P3	-.96	0.70	.000	MV2-MV3	1.23	1.25	.000

(RI)stands for Resistivity index, (PI)for pulsatility index (MV) for Mean Velocity in all of the studied groups in first , second and third trimester(RI1,RI2,RI3 and PI1,PI2,PI3 and MV1,MV2,MV3)

Table (4.8) : T-test showed the difference between the measured values for Resistivity index (RI), pulsatility index(PI), Mean Velocity (MV) comparison between the examined groups and normal healthy pregnant ladies in the three trimesters.

	Site	Parameters	Smoker pregnant Ladies	Diabetic Ladies	Smoker Diabetic Pregnant Ladies
Normal Pregnancy	Left Eye	R1	0.003	0.000	0.000
		RI2	0.025	0.000	0.000
		RI3	0.038	0.000	0.000
	Right Eye	R1	0.000	0.000	0.000
		RI2	0.000	0.000	0.000
		RI3	0.000	0.000	0.000
	Left Eye	PI1	0.000	0.000	0.000
		PI2	0.000	0.000	0.000
		PI3	0.000	0.000	0.000
	Right Eye	PI1	0.000	0.000	0.000
		PI2	0.000	0.000	0.000
		PI3	0.000	0.000	0.000
	Left Eye	MVI	0.000	0.000	0.000
		MV2	0.000	0.000	0.000
		MV3	0.000	0.000	0.000
	Right Eye	MVI	0.000	0.000	0.000
		MV2	0.050	0.020	0.000
		MV3	0.010	0.044	0.000

Correlation is significant at $p \leq 0.05$

Chapter Five

Discussion, Conclusion

&

Recommendations

CHAPTER FIVE

DISCUSSION

5.1 DISCUSSION

5.1.1 Discussion Of Maternal Ophthalmic Artery Doppler Indices In Type 1 Diabetes During Pregnancy:

This Study aimed to assess the Doppler indices for ophthalmic artery in type 1diabetic pregnant ladies. As shown in table 4-1, For diabetic pregnant ladies Mean RI ,PI ,MV were found to be 1.3 ± 0.5, 3.0 ± 1.6, 5.8 ± 1.7,for left eye and 1.2 ± 0.5, 3.2 ± 1.6, 5.4 ± 2.1 for right eye, Doppler Indices as RI ,PI were increased in the left and right eye significantly in second and third trimester at *p* value= 0.000,where MV were decreased significantly .

The study indicates that ophthalmic artery Doppler parameters in pregnant women at risk for diabetes are different from the reference values that have been reported from healthy pregnancies. (R.S .Carneiro et al2008), (A.L. Diniz et al2005)(F .Mackenzie et al1995) The diabetic pregnant ladies were treated with insulin or diet control .The study showed that there was no significant difference between the type of treatment and (RI, PI & MV) in left or right eye as seen in table 4-2.

Describing the effect of diabetes is that the elevated glucose levels are important factor leading to alterations of vessel architecture in the retina, flow irregularity, and development of the disease. Changes of retinal vessels include thickening of the capillary basement membrane,(J. Cai et al 2002) Capillary hypo perfusion.(L .Schmetterer et al 1999) These justify the increasing of RI and PI and reduction of MV.

Similar investigators have reported that blood flow velocities in the retro bulbar central retinal artery (T .Kawagishi et al 1995) and in branch retinal arteries are reduced. (G T .Feke et al. 1994)

Regarding the results, both pregnancy and diabetes can cause retinopathy, due to the noticeable changes of Doppler indices. Table (4.3) showed significant differences in the indices in the second and third trimester for right and left eyes in healthy pregnant ladies. During pregnancy, physiological changes occur in the vessels (G T .Feke et al 1994)pregnancy causes weakening in the retinopathy conditions in diabetic women, even when good metabolic control is achieved and retinopathy is minimal. (G . Soubrane et al 1985) (T. Hellstedt et al 1996)

The main finding of the study was that retinal mean blood flow velocity was 5.8 which is higher in women with insulin-dependent diabetes than in diet control. Similar results were found in previous studies.(Sirpa Loukovaara et al 2003)

In contrast, no tendency towards an increase in mean retinal blood velocity flow was seen in the pregnant non diabetic ladies .In addition, a significant difference existed in Doppler indices of right and left eyes between pregnant non diabetic, and diabetic pregnant and control subjects as seen in table (4.4) whereas pregnant diabetic women had higher RI, PI values and lower MV values than did pregnant non diabetic and control subjects.

We noticed that pregnancy itself may cause retinopathy. This consigned to what was stated that after accounting for glycemic control, the pregnancy state itself was a major risk factor of retinopathy. (D.C.2000)Various factors have been shown to influence the progression of diabetic retinopathy during pregnancy. These included the pregnant state itself, duration of diabetes prior to the pregnancy, degree of retinopathy at time of conception, metabolic control before and during pregnancy, as well as the presence of coexisting hypertension. (L.P. Aiello et al 2000). These results showed similar findings done by(Schocket et al.1999)who found a decrease in retinal volumetric blood flow during the third trimester in both diabetic and non-diabetic mothers, with larger significant decrease in diabetics. This group speculate the progression of diabetic retinopahy.(L.P. Aiello et al 2000)exist before the clinical

development of diabetic retinopathy in pregnant ladies with type1diabetic.
Our agreements were consistent with the recommendations of the American Diabetes Association (L.P. Aiello et al 2000) which recommend that women with preexisting diabetes who are planning a pregnancy should have a comprehensive eye examination and be counseled on the risk of development and/or progression of diabetic retinopathy.

5.1.2 Discussion Of A Study Of Maternal Ophthalmic Artery Doppler Indices In Diabetics And Smokers

This study analyzed the correlation between ophthalmic Doppler indices and gestational age (pregnancy trimesters) in healthy ladies with singleton pregnancies. In normal pregnant ladies group the RI, PI, MV were measured in each trimester for both eyes . As shown in table4.5 and (table4.6),No significant difference was detected between RI in first trimester and RI in the second trimester for the left eye, while the readings in the second trimester for RI2-RI3,PI1,PI2,PI3 and MV1,MV2,MV3 showed significant difference for both left and right eyes.

Previous studies assessed the orbital circulation using ultrasonography, and patterns of orbital vessels normality have been described. The importance of this examination was first shown in ophthalmologic diseases. (Erickson SJ et al 1989) ,(Lieb WE et al 1991).

Before abnormalities can be recognized in the eye , measurements must be achieved in healthy pregnant ladies, and the variation affecting the normal data should be resoluted. Therefore the current study analyzed the correlation between ophthalmic Doppler indices (RI, PI, and MV) and GA progress in healthy patients with singleton pregnancies.

Hata et al 1992)were the first to use Doppler velocimetry of the ophthalmic artery in the assessment of pregnant women. Several authors have

since evaluated this method during pregnancy, especially in patients with hypertension. (Ayaz T et al 2003), (Ohno Yet al 1999),(Carneiro RS et al 2008) Ocular Doppler sonography has been shown to be an perfect, objective, and capable method in the evaluation of preeclampsia .Yet, agreement on the reference values for the flow parameters of ocular Doppler sonography in normal pregnancy has not yet been established. (Barbosa AS et al 2004) When comparing our results with the previous similar studies,(MacKenzie et al 1985) evaluated ophthalmic Doppler indices in normal pregnant ladies and reported that the ophthalmic artery (RI) decreased, whereas the (PI) remained unchanged with advancing gestational age (GA).However,(Ohno et al 1999) reported an inverse correlation between PI and GA values in normal pregnant ladies, and (Carneiro et al 2008)and reported no significant correlation between Doppler indices (including the RI and PI) in healthy pregnant women. Also(Cristiane et al 2008) reported that there was no significant differences were found between the values obtained for the first and the second measurements in each eye and those for the RI, PI, and PR in the right and left eyes. But There was a significant decrease in RI and PI values with advancing GA.

In the second group, (the smoker pregnant ladies) we found that the changes of RI,PI for the left eye did not differ significantly as the GA increased , however significant changes were detected for all of the parameters (RI,PI,MV) in the second and third trimesters for both eyes .However no significant changes between PI1 and PI2 of the right eye in smoker pregnant ladies $p \leq .531$. In the fourth group (the smoker diabetic pregnant ladies); Doppler indices for RI,PI,MV were statistically differ as the gestational age increased except for PI in the second trimester (Table 4.6),(Table4.7).When comparing the normal pregnant values(Controls) with the(Salafia C et al 1999)smoker pregnant ladies and the smoker diabetic pregnant ladies ; a significant difference were detected in all trimesters (Table4.8).

The effects of smoking on the vessels are due to vasoactive substance inhaled(Salafia C et al 1999) Doppler indices of OA allocate us to characterize the hemodynamic changes in vessel. In the current study, we evaluated the readings of the Doppler indices in the OA and compared the findings with normal pregnant ladies readings.(table4.8)

There are few studies characterizing the effects of cigarette in OA and they all didn't discuss the effects in pregnant ladies.[86-90]

Researchers, assessing the effects of smoking, observed lower peak systolic velocity in OA of smokers without change in end diastolic velocity and RI, compared to controls,(Steigerwalt Jr RD et al 2000) but other researchers, report that the peak systolic velocity was lower in smokers. (Williamson TH et al 1985) These two authors did not specify how long ago was the use of cigarettes(Williamson TH et al 1995) ,(Steigerwalt Jr RD et al 2000), (Similarly; our study did not consider the duration of smoking nor the type (cigarettes,sigar ,shisha, handmade cigarettes (tobacco roll), or other sourse of tobacco smoking) or the numbers of cigarettes/day in all individuals in the two groups. We correlated the variables in each trimester, our findings was in disagreement with those studies.

In previous studies about the Doppler velocimetry in smokers, the RI and PI show the arterial resistance to blood distal flow, reflecting vasoconstriction and hypoperfusion. Low PI values indicate ophthalmic artery hyperperfusion and hyperaemia. (Thompson RS et al 1988), (Ohno Y et al 1999),A study evaluated smokers in advanced phase of using up, found an association between smoking and changes in blood flow in the ophthalmic artery (Ergýn A et al 2005)they found that the mean Doppler values were consistent with hypoperfusion, with low peak systolic velosity and higher RI compared to controls.

Other studies, found results consistent with vasodilatation, with higher peak systolic velosity lower RI compared to controls (Kaiser HJ et al 1997),(Satici A et al1999)These studies, are not in concordance with our results. We justify our results of finding the correlation between smoking and ophthalmic artery perfusion pattern is that there is signs of vasoconstriction. Our results finding reflects that the OA Doppler indices in smokers is compatible with hypoperfusion and vaso constriction. In diabetic pregnant ladies group; there are significant increasing in RI as the GA increased for both right and left eyes as well as the PI and MV was found to be significantly changed in second and third trimester.(table4.6),(table4.7). When comparing the third group (diabetic pregnant ladies) with controls significant differences were detected between the diabetics and normal pregnancy (table4.8).

Studies have mentioned that the association of smoking and diabetic retinopathy has not been clear . (Sang AhChang et al 2012)It was reported that retinopathy has been associated with glycemic control and not smoking state.(Guillausseau PJ et al 1995) Some studies have reported no association with smoking and retinopathy in type 2 diabetes. Moss SE et al 1996), (Guillausseau PJ et al 1998), The United Kingdom Diabetic study was done to determine risk factors related to the incidence and progression of diabetic retinopathy . The development of retinopathy was associated with glycemia and higher blood pressure, but not smoking.(Stratton IM et al 2001) Thus in type 2 patients, the effects of smoking on diabetic retinopathy is not clear. (Sang AhChang et al 2012).

Using color Doppler sonography, Mendivil and associates (1995)and Mendivil and Cuartero(1996)reported that ocular blood flow velocity was decreased in diabetic patients with diabetic retinopathy . This was in concordance with our results.

In a study done by(Khan.et al 2014) , peak systolic velosity was increased in diabetic. Reduced cellular oxygenation in diabetes may demand a compensatory increase in vascular flow. (Numata K et al 1997) This justified

our result is that the MV was increased .Increasing in RI in our study may be due to downstream vascular changes related to diabetes. (Numata K et al 1993)

Regarding the results (highly significant changes of Doppler indices in group four during the pregnancy period) it showed that smoking has harmful effects on patients with diabetes. Smoking increases diabetic incidence and aggravates glucose homeostasis and chronic diabetic complications.

5.2 Conclusions

Readings Of Ophthalmic artery Doppler indices (resistive index (RI), pulsatility index (PI)) for type 1diabetes ladies were found to be greater when compared with reference values mentioned in the literature and the control group values and Mean Velocity (MV) was of lower values. The study recommended to consider changes RI and PI values in all the pregnancy periods which reflect the critical phase that exist before the clinical development of diabetic retinopathy in pregnant ladies with type1diabetic.The study agreements were consistent with the recommendations of the American Diabetes Association(L.P. Aiello et al 2000) which recommend that women with preexisting diabetes who are planning a pregnancy should have a comprehensive eye examination and be counseled on the risk of development and/or progression of diabetic retinopathy.

Smoking provokes perfusion changes in ophthalmic artery in smoker pregnant ladies. Thus, there are signs of an ophthalmic artery vasoconstriction and hypoperfusion. OA blood flow velocity was decreased in diabetic patients.

5.3Recommendations

- Role of Doppler Ultrasound should not be neglected as it gives good idea about the progression and regression of the underlying eye complication due to diabetes.
- Regular follow up is cornerstone in early detection and management of many eye complication due to diabetes.
- Good control of pre-existing diabetes and hypertension plays an important role in preventing severe eye complications.
- smoking must be avoided as it worsen the outcome of pre-existing eye complication.
- Diabetics can also greatly reduce the possibilities of eye complications by scheduling routine examinations with an ophthalmologist. Many problems can be treated with much greater success when caught early.
- Ladies should be aware about the risks of uncontrolled diabetes and smoking if they are planning for pregnancy .They must stop smoking and visit physician for controlling their blood sugar to avoid any complication in futures.
- For more accurate results, future studies should address more about relationship between smoking, pregnancy and diabetes.

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Appendices

Appendix A

THE DATA COLLECTED DURING THE STUDY

Name:……..

Age:……..

Duration of Disease:…….……..

Type of Treatment:

Insulin( ) Tablets( ) Diet control( )

Treatment:

Regular( ) Not regular( )

U/S Findings: (Gray Scale):

Rt Eye:

The Lens:…….

The Vitrous Gel:…….

The Retina:……..

Lt Eye:

The Lens:…….

The Vitrous Gel:…….

The Retina:…….

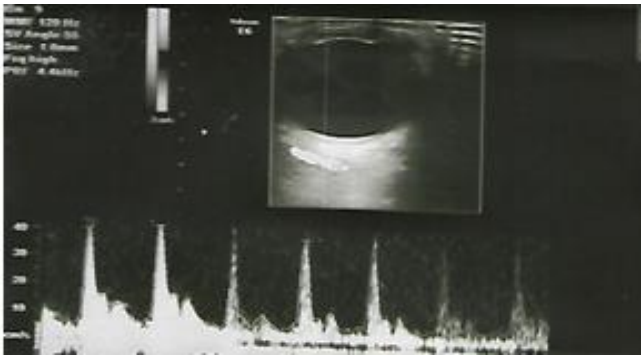
Colour Doppler: (Opthalmic Artery):

Rt Eye: RI:……PI:……Mv:……..

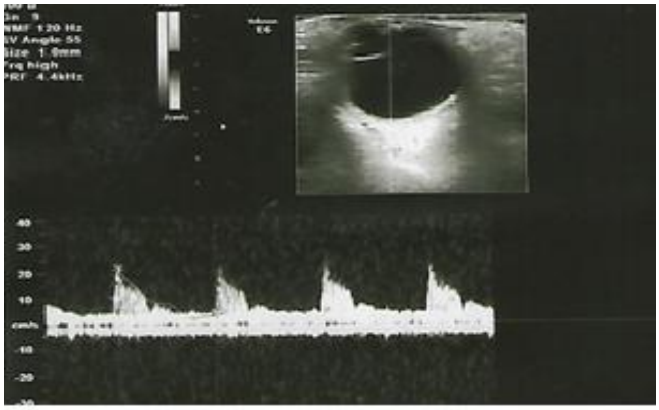
Lt Eye: RI:……PI:……Mv:…….

Appendix B

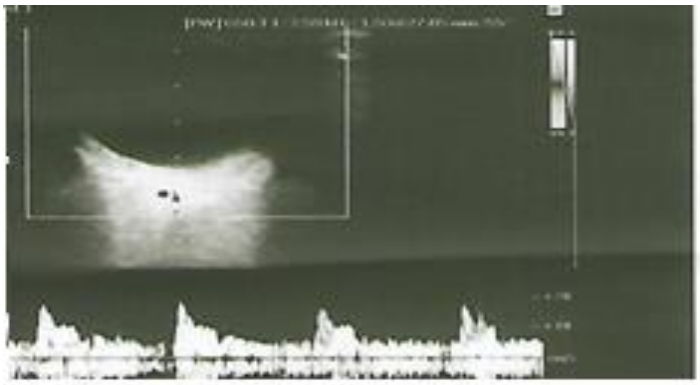
ULTRASOUND IMAGES



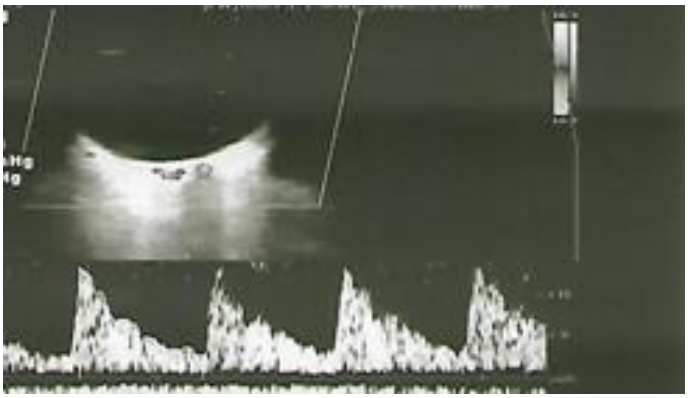
B1: Normal flow of Opthalmic artery.



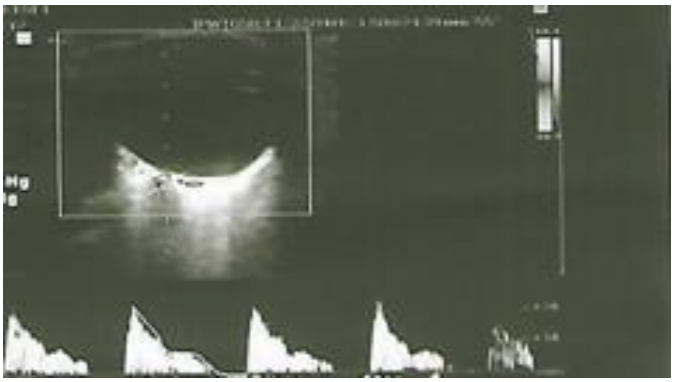
B2:Ophthalmic artery wave in patient with type 1 diabetes.



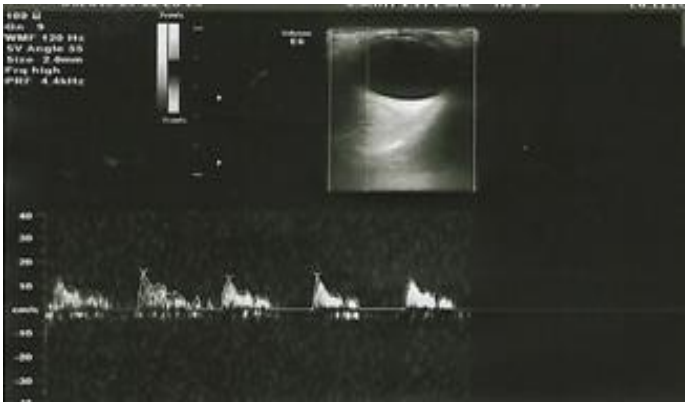
B 3: Ophthalmic artery wave in smoker pregnant ladies.



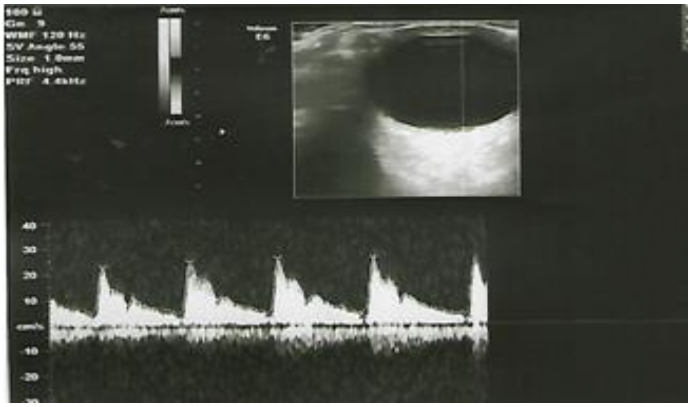
B4: Opthalmic artery flow of healthy pregnant ladies.



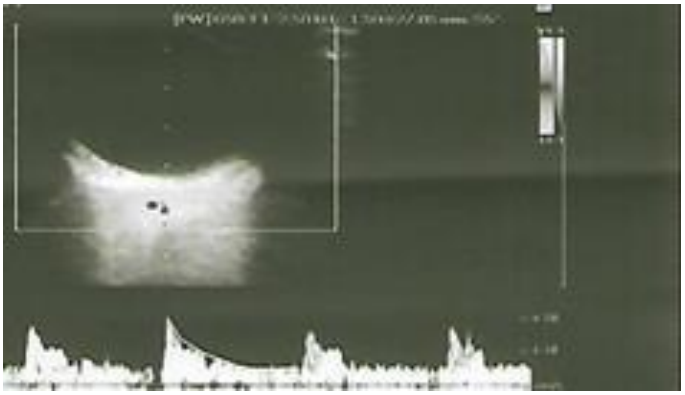
B5: Ophthalmic artery wave in diabetic smoke pregnant ladies.



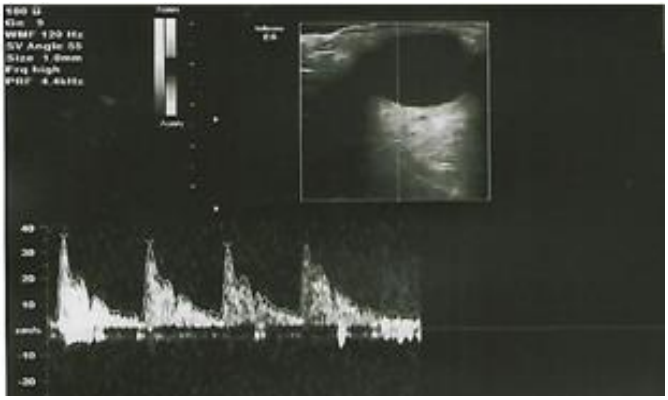
B 6: Ophthalmic artery wave in diabetic smoke pregnant ladies.



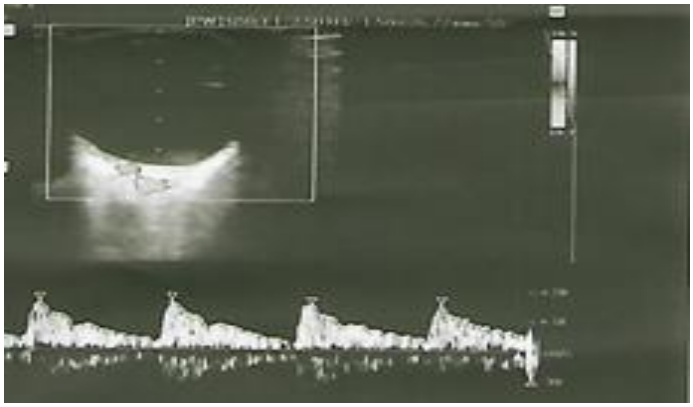
B 7: Opthalmic artery flow of healthy pregnant ladies.



B8: Ophthalmic artery wave in smoker pregnant ladies.



B9: Normal colour Doppler and wave of an Opthalmic artery.



B 10: Ophthalmic artery wave in ladies with type 1 diabetes