A COMPARATIVE STUDY OF CENTRAL CORNEAL THICKNESS IN DIABETICS AND NON-DIABETICS USING ULTRASONIC PACHYMETRY

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In

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I hereby declare that this dissertation/thesis entitled "A COMPARATIVE STUDY OF CENTRAL CORNEAL THICKNESS IN DIABETICS AND NON-DIABETICS USING ULTRASONIC PACHYMETRY" is a bonafide and genuine research work carried out by me under the guidance of DR. **M. H. PATIL. M.S.** (Ophthalmology) Professor, Department of Ophthalmology, B.L.D.E (Deemed to be University), Shri B.M. Patil Medical College, Hospital and Research Centre, Vijayapura, Karnataka.

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LIST OF ABBREVIATIONS

CCT	Central corneal thickness
LASIK	Laser in-situ keratomileusis
T2 DM	Type 2 diabetes mellitus
IOP	Intraocular pressure
μ	Micron
FPG	Fasting plasma glucose
OGTT	Oral glucose tolerance test
NPDR	Non proliferative diabetic retinopathy
PDR	Proliferative diabetic retinopathy
AGEs	Advanced glycosylation end products
ORA	Ocular Response Analyzer
CH	Corneal hysteresis
CRF	Corneal resistance factor
OCT	Optical coherence tomography
UBM	Ultrasound bio microscopy
RBS	Random Blood Sugar
FBS	Fasting Blood Sugar
PPBS	Post Prandial Blood Sugar

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ABSTRACT

BACKGROUND

Central corneal thickness (CCT) is an important indicator of corneal health status. Thicker and thinner corneas may lead to either overestimation or underestimation of intraocular pressure, which is the most important causal and treatable risk factor for glaucoma. The findings in the previous studies on the association between diabetes and CCT are conflicting. CCT may also influence outcome in cataract and refractory surgeries.

AIM

The aim of the study is to determine an association between central corneal thickness and type 2 diabetes mellitus (T2 DM).

MATERIALS AND METHODS

This is a cross-sectional and time-bound study carried out on patients attending the outpatient and inpatient departments of Ophthalmology, B.L.D.E.(DU)'s Shri B.M. Patil Medical College, Hospital and Research Centre, Vijayapura. The study includes 168 adult subjects divided into three groups:

a. 40 patients with Type 2 Diabetes Mellitus for duration more than 10 years
b. 46 patients with Type 2 Diabetes Mellitus for duration less than or equal to 10 years
c. 82 controls

Details of the patient including history, clinical examination, investigations are recorded after obtaining consent from the patient. Clinical examination includes

Visual Acuity (by Snellen's Chart), Slit Lamp Examination, Dry and Cycloplegic (if required) retinoscopy with streak retinoscope, subjective correction, Pachymetry (Ultrasound), B-Scan (if required) and intraocular pressure (by applanation tonometry).

RESULTS

A total of 168 patients were included in the study. A highly statistically significant difference was found between the mean central corneal thickness of diabetics (534.0581µ in right eye and 534.3605µ in left eye) and non-diabetics (525.8659µ in right eye and 525.8659µ in left eye), as the computed 'P' value through ANOVA (0.000726) is less than 0.05. Association between central corneal thickness and age, gender, laterality and duration of diabetes were not statistically significant.

CONCLUSION

A statistically significant difference in CCT was found between diabetics and non-diabetics. Henceforth, it is important to measure the central corneal thickness in all diabetics, as it affects the IOP measurement which is vital for early diagnosis and timely treatment of glaucoma.

INTRODUCTION

Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease. In 2000, India (31.7 million) topped the world with the highest number of people with Diabetes Mellitus. According to Wild et al. the prevalence of Diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India i.e. 79.4 million. [1]

Worldwide, the incidence of Type2 Diabetes Mellitus is increasing, reaching epidemic proportions in developing countries. The disease entity is characterized by hyperglycemia and the development of micro-macro vascular disorders, leading to functional and morphological disorders in several organs. Ocular manifestations include anterior ischemic neuropathy, glaucoma, cataract, retinal vein and arterial occlusions and retinopathy/maculopathy. The development of many of the diabetic complications is related to duration of the disease and the degree of metabolic dysregulation. [2-4]

Several studies have indicated changes in human corneal endothelial cell morphology in patients with Type2 Diabetes Mellitus. [2,5-7] Hypothetically, these phenomena could be caused by chronic metabolic changes at the cellular level that primarily affect the single layer of coherent endothelial cells. [2,8] These largely hexagonal cells have practically no proliferative activity. They are responsible for maintaining the hydration of the stroma by actively removing water, thus playing a pivotal role in maintaining the transparency of the cornea. [2]

The central corneal thickness is a sensitive indicator of health of cornea and serves as an index for corneal hydration and metabolism. Thicker and thinner corneas may lead to either overestimation or underestimation of intraocular pressure, which is the most important causal and treatable risk factor for glaucoma. It is also an important indicator of patency of corneal endothelial pump and can be objectively measured by a variety of techniques like optical pachymetry, ultrasound pachymetry, confocal microscopy, ultrasound bio microscopy, optical ray path analysis or scanning slit corneal topography and optical coherence tomography. Ultrasound pachymetry is the current standard for corneal thickness measurement. As per a study done in 2008 in Malay individuals, central corneas were significantly thicker in patients with diabetes than in those without diabetes (547.2 micron vs.539.3micron, $p<0.001$). [9]

Factors influencing the corneal pachymetry include the time of the day, patient age, the use of contact lens, or any corneal degeneration.

NEED FOR THE STUDY:

The effect of diabetes on corneal thickness has not yet been clearly established. Few studies state that the central corneal thickness is unaffected by diabetes, while few studies state that central corneal thickness would significantly increase in diabetics when compared to non-diabetics. Moreover, the studies on this subject in the Indian population are quite a very few. This necessitated further evaluation of the association between central corneal thickness and diabetes mellitus.

AIM OF THE STUDY

AIM OF THE STUDY

To study central corneal thickness in diabetics and non-diabetics using ultrasonic pachymetry.

REVIEW OF LITERATURE

Diabetes mellitus

Definition

"Diabetes mellitus is now defined as a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both." [10]

Epidemiology of diabetes mellitus

Global

There is a worldwide rise in the incidence of diabetes mellitus reaching epidemic proportions in developing countries like India and China. As per the WHO global report on diabetes, the prevalence of diabetes mellitus worldwide among adults has mounted from 4.7% in 1980 to 8.5% in 2014. [11]

India

India (31.7 million) had the maximum number of people with diabetes mellitus followed by China (20.8 million) in the year 2000. [1]

According to Wild et al. the prevalence of diabetes mellitus is expected to double globally from 171 million in the year 2000 to 366 million in the year 2030 with the highest rise in India. Also, there is a prediction that, diabetes mellitus may affect up to 79.4 million people in India, 42.3 million in China and 30.3 million in the United States by the year 2030. [12] [13]

Classification of diabetes mellitus

Diabetes mellitus is classified into the following categories

1. Type 1 diabetes - It occurs due to β-cell destruction resulting in insulin deficiency.
2. Type 2 diabetes - It occurs due to a defect in insulin secretion & insulin resistance.
3. Gestational diabetes mellitus (GDM) – It is not overt diabetes and it is diagnosed in the 2nd or 3rd trimester of pregnancy.
4. Specific types of diabetes – Ex: due to diseases of the exocrine pancreas, monogenic diabetes syndromes, chemical-induced diabetes [14]

Type 2 Diabetes ADA Diagnostic criteria

"The American Diabetes Association Expert Panel recommends a diagnosis of diabetes mellitus when 1 of the following 4 criteria are met and confirmed with retesting on a subsequent day:

- HbA1c ≥6.5% (<5.7% = normal)
- FPG level ≥126 mg/dL (7.0 mmol/L)
- 2-hour plasma glucose level ≥200 mg/dL (11.1 mmol/L) with 75-g OGTT
- Random plasma glucose level ≥200 mg/dl (11.1 mmol/L) in a patient with classic symptoms of hyperglycaemia, including polyphagia, polyuria, and polydipsia." [15]

Effects of hyperglycemia on the eye

Lids/Lashes

Diabetic patients are more prone for infections and hence at a higher risk of developing blepharitis [16], orbital cellulitis [17], recurrent hordeolum. [18]

Conjunctiva

According to a study conducted by Siefart et al, 86% of diabetics showed pathological changes in conjunctiva. [19]

Another study reported an increase in squamous metaplasia and reduction in the density of goblet cells in diabetics. [20,21]

Cornea

Various structural and physiological changes occur in diabetics and are discussed elaborately later.

Iris

One of the most deleterious effect on iris is neovascularization. It is often present around the pupillary margin but in advanced cases, it may involve the angle of anterior chamber and even the whole of iris. [22] These changes result in neovascular glaucoma.

Depigmentation of iris epithelium occurs which results in the release of pigments. [23]

Pupil

Diabetics present a small pupil with normal light reflexes because the sympathetic nerve supply is affected. [24] Histological studies on irides revealed loss of nerve

terminals from the dilator muscle. [25] Small pupil causes intraoperative difficulties leading to more manipulations of the pupil during surgery, which can result in excessive postoperative inflammation.

Changes in refraction and lens

Furushima et al conducted a study in Otia, Japan to establish changes in refraction in healthy subjects by inducing an acute hyperglycemic state. The purpose of the study was to determine changes in intraocular pressure and myopia after a load of glucose. Oral glucose tolerance tests were performed on 7 healthy young volunteers with normal visual acuity. After the glucose load, hematologic parameters and changes in the refractive system were measured periodically for 150 minutes. After the glucose load, a raise was observed in the plasma glucose level, plasma osmosis level, myopic change in refractive power, ocular hypotension and thickening of lens. Power of residual accommodation was excelled by the degree of myopic change. Normalization of plasma glucose level resulted in normalization of intraocular pressure and reversal of myopic changes. These findings suggest that the myopic changes associated with hyperglycemia were caused by lens thickening, which was due to a reduction in the tension of the zonular fibers of Zinn. [26]

Wiemer et al reported that diabetes has an effect on the refractive power of posterior cornea, but the total corneal refractive power remained unaffected. This suggests that the refractive changes in diabetics were due to changes in lens. [27]

Diabetics have an increased risk of early onset cataracts. Many large population studies such as Blue Mountains Eye Study [28] and Beaver Dam Eye Study [29] reported an increased incidence and prevalence of posterior subcapsular cataracts in diabetics.

The following are the hypotheses which explain lens changes in diabetics

1. The first mechanism is increased flux mediated by aldose reductase.

2. The second mechanism is glucose mediated activation of a specific isoform of protein kinase C that results in early onset cataracts in diabetics.

3. The third mechanism is increase in the production of advanced glycation end products (AGEs), which are produced by the non-enzymatic reaction of aldehydes such as glucose. [30]

Aqueous humor

According to some studies, the effect of diabetes on aqueous humor dynamics is not consistent, while some studies reported a decreased rate of aqueous humor formation in diabetics. [31-32] Few studies reported that this decreased aqueous humor secretion is mild and not clinically significant [33]

Vitreous

Non-enzymatic glycation and abnormal collagen crosslinking [34] occur in the vitreous of diabetics which can result in posterior vitreous detachment (PVD) and precocious vitreous liquefaction. [35-36]

Retina

Small vessels become vulnerable to damage in diabetic microangiopathy due to hyperglycemia. Also, retinal cells are directly affected by hyperglycemia.

1. The following are the mechanisms of cell death

a. Intracellular sorbitol accumulation,
b. activation of a specific isoform of protein kinase C,
c. oxidative stress due to radical excess,
d. increased production of advanced glycation end products.

A salient early feature is disruption of ion channel function.

2. Damage to the retinal capillaries is marked by the death of pericytes, loss of vascular smooth muscle cells, thickening of the capillary basement membrane and proliferation of the endothelial cells.
3. Haematological abnormalities seen are erythrocyte and leucocyte abnormalities, increased platelet adhesion and increased plasma viscosity. This results in capillary leakage and occlusion.
4. Capillary non perfusion results in retinal hypoxia, which in turn leads to neovascularization. Neovascularization extends both preretinally and intraretinally, where intraretinally they are referred to as intraretinal microvascular abnormalities. Imbalance between angiogenic and anti – angiogenic factors is the cause for this new vessel growth. Various angiogenic factors such as vascular endothelial growth factor, platelet derived growth factor and hepatocyte growth factor are produced to revascularize hypoxic retina. [37]

Brownlee M in his study on biochemistry and molecular cell biology in the evolution of diabetic retinopathy reported that increased polyol pathway flux, increased advanced glycation end products (AGEs), activation of a specific isoform of protein kinase C (PKC) and increased hexosamine pathway flux are the mechanisms responsible for diabetic retinopathy. [38]

Diabetic retinopathy is broadly categorized into non proliferative diabetic retinopathy and proliferative diabetic retinopathy.

In non-proliferative diabetic retinopathy, there is development of microaneurysms, dot and blot hemorrhages, exudates and venous changes. It is a stage prior to proliferative diabetic retinopathy.

Proliferative diabetic retinopathy is marked by the formation of new blood vessels on or within 1disc diameter of the optic disc and /or formation of new vessels elsewhere in the fundus. (39)

Cornea

Cornea is a transparent and avascular tissue. It consists of 6 layers from anterior to posterior:

- Epithelium,
- Bowman's membrane,
- Stroma,
- Dua's layer
- Descemet's membrane &
- Endothelium.

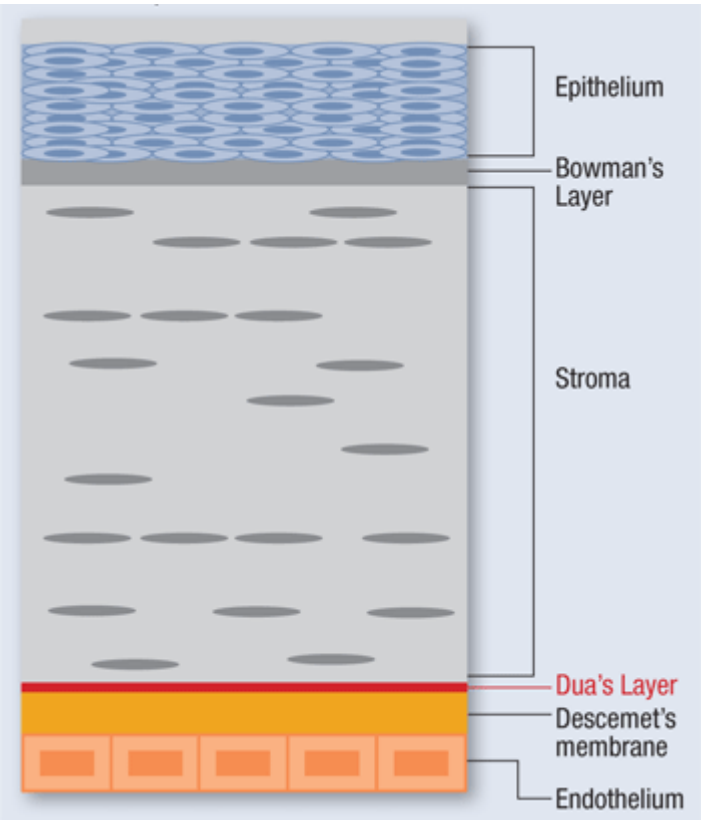


Fig 1: Layers of cornea

It measures 11–12 mm horizontally and 10–11 mm vertically in adults. At the centre, it is approximately 500–600 μ thick and increases in thickness gradually towards the periphery.

Corneal Epithelium

The corneal epithelium consists of 4–6 layers. Superficial 1–2 layers are squamous cells, then 2–3 layers of broad wing cells and the innermost is the layer of columnar basal cells. It is 40–50 μ thick. An optically smooth surface is formed by the epithelium and tear film. Penetration of tear fluid into the stroma is prevented by tight junctions between superficial epithelial cells. Other layers arise from the continuous proliferation of the limbal stem cells, which subsequently differentiate into superficial cells. These differentiated cells become coated with microvilli on the outermost

surface with maturation & then they desquamate into tears. Differentiation approximately takes 7–14 days. Basal epithelial cells produce a continuous, 50- nm-thick basement membrane, which is made up of type IV collagen, laminin & other proteins. Corneal clarity depends on the tight packing of epithelial cells.

Bowman Layer

Anterior to the corneal stroma lies bowman's layer. It is an acellular condensate of the anterior most portion of the stroma. It is 15 μ thick and maintains the shape of the cornea. It does not regenerate.

Corneal Stroma

90% of the total corneal thickness is constituted by the corneal stroma. For a clear cornea, the regular arrangement of stromal cells (keratocytes), fibers and extracellular matrix is necessary. Keratocytes differ in size and density & form a 3-dimensional network throughout the cornea. They are located between the stromal collagen lamellae and are flattened fibroblasts. They continuously digest and produce stromal molecules. The density of keratocytes declines with age, by 0.9% per year for anterior density & 0.3% per year for posterior density. It also decreases with refractive laser surgery.

The corneal stroma consists of an extracellular matrix made of collagens and proteoglycans. Type I & type V fibrillar collagens are entwined with filaments of type VI collagen. Major corneal proteoglycans are decorin (associated with dermatan sulfate) & lumican (associated with keratan sulfate).

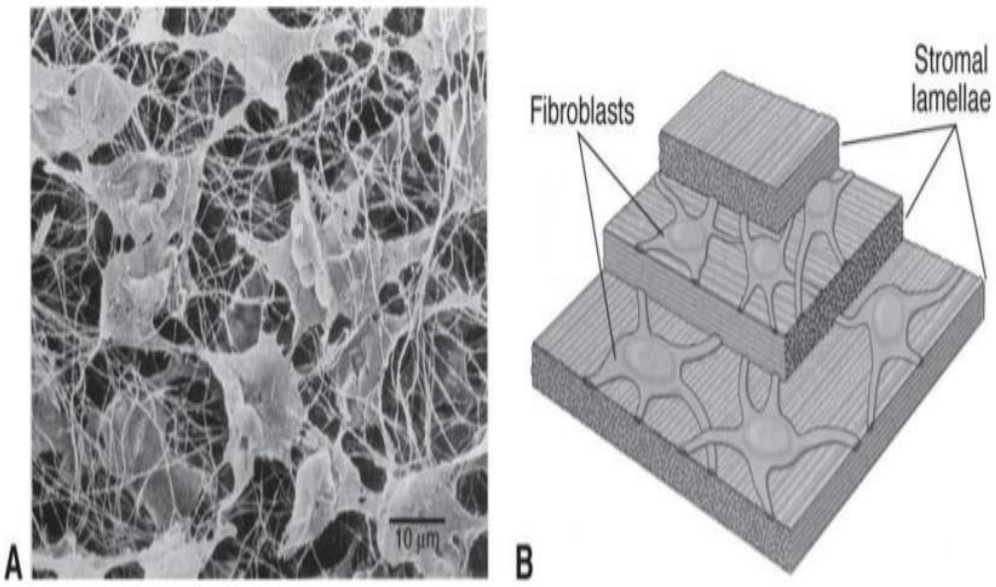


Fig 2: Keratocytes are flattened fibroblasts situated between the stromal lamellae

Corneal transparency is maintained by regulating the water content of corneal stroma at 78%. Intact epithelial and endothelial barriers and endothelial pump functioning, which is linked to an ion-transport system regulated by temperature dependent enzymes such as Na+, K+-ATPase maintain corneal hydration. Stromal glycosaminoglycans, which are negatively charged repel each other, resulting in a swelling pressure (SP). Since the intraocular pressure (IOP) tends to compress the cornea, the total imbibition pressure of the corneal stroma is taken as IOP – SP. Corneal hydration changes from anterior to posterior and increases closer to endothelium.

Descemet Membrane

The Descemet membrane is considered as the basement membrane of the corneal endothelium. It is 3 µ at birth & increases in size to 10–12µ by adulthood. This is because the endothelium gradually lays down a posterior amorphous, non-banded

zone. Though controversial, a novel layer called **pre-Descemet layer or Dua's layer** in the posterior part of the cornea has been reported. This layer may be of importance while performing deep anterior lamellar keratoplasty. The Schwalbe line defines the end of Descemet membrane and the beginning of trabecular meshwork and it's a gonioscopic landmark.

Corneal Endothelium

Corneal endothelium is composed of a single layer of closely interdigitated cells organized in a mosaic pattern of mostly hexagonal shapes. Human endothelial cells do not proliferate in vivo, but they can divide in cell culture. In case of cell loss, especially due to trauma or surgery, the defective area is covered by the enlargement and spread of residual cells or perhaps peripheral stem cells. These cell findings can be noted on specular microscopy as polymegathism (variability in cell size) & polymorphism (variability in cell shape). The endothelial cell concentration is highest at the periphery. Central endothelial cell density declines with age at the rate of approximately 0.6%/year. It reduces from a count of about 3400 cells/mm2 at age 15 years to about 2300 cells/mm2 by age 85 years. The normal central endothelial cell count is between 2000 and 3000 cells/mm2. Those eyes with an endothelial cell count below 500 cells/mm2 are at risk of corneal edema. The endothelium maintains corneal transparency by regulating corneal hydration and maintains stromal deturgescence by its barrier function to the aqueous humor & by its metabolic pump function, that moves ions and draws water osmotically, from the stroma into the aqueous humor. Decreased endothelial cell density causes increased permeability and insufficient pump functioning resulting in clinically evident edema.

Both structural and functional changes in cornea have been studied and reported in diabetics. Diabetics are at a higher risk of various corneal complications such as superficial punctuate keratitis, persistent epithelial defects, recurrent corneal erosions, corneal endothelial damage. [40-42] These corneal complications are associated with tear film abnormalities, improper adhesion between epithelial cells and the basement membrane and reduced corneal sensations. [40], [43]

Changes in corneal biomechanical properties and corneal thickness have also been reported. Cornea, in total has five layers. The major bulk (up to 90% of its thickness) of cornea is the stroma which is externally bounded by bowman's membrane and epithelium, internally bounded by Descemet's membrane and endothelium. Cornea is composed of 78% water, 15%collagen, 5%other proteins, 0.7% keratan sulphate, 0.3%chondroitin sulphate, 1% salts. [44]

REVIEW OF FEW RELATED STUDIES

Studies on changes in corneal epithelium and endothelium:

Taylor et al obtained corneas from 12 donor eyes of patients with maturity-onset diabetes mellitus and studied corneal epithelial basement membranes by transmission electron microscopy. Similar tissue was obtained from 12 donor eyes from age matched (within 2 years) and race matched nondiabetic individuals. The mean corneal epithelial basement membrane thickness in nondiabetic individuals was 0.33 fim (±0.11 S.D.), which gives a normal range of 0.11 to 0.55 fim. None of the nondiabetic basement membranes lie outside this range. The basement membranes of 4 out of the 12 diabetic patients exceeded this range of thickness. No sex difference or race difference was noted in the basement membrane thickness. And no clear trend was observed with age. Eight diabetic patients and six nondiabetic patients showed multilaminate basement membranes. This suggests that multilamination was more related to basement membrane thickness than to the absence or presence of diabetes. (45)

Choo et al did a hospital based observational study in which they included 200 eyes from 100 controls and 100 type II diabetic patients and they used specular microscopy and pachymetry to measure endothelial cell density, size, hexagonality, coefficient of variation in cell area and corneal thickness. It was observed that endothelial cell density in the diabetic group (2541.6± 516.4 cells/mm2) was strikingly lower than that of the control group (2660.1± 515.5 cells/mm2). (46)

Lee et al compared the corneal thickness and corneal endothelial morphology of diabetics with age matched healthy control subjects. They performed ultrasound pachymetry and noncontact specular microscopy on 100 control subjects and 200

patients with diabetes. A partial correlation 24 coefficient was used to find correlation between subject parameters and duration of diabetes. It was found that the diabetics had thicker corneas, less hexagonality and cell density and more irregular cell size of the corneal endothelium when compared to controls. Central corneal thickness and the coefficient of variation for cell size were significantly higher in diabetics of over 10 years' duration when compared to diabetics of less than 10 years' duration. The corneal endothelial cell density and percentage of hexagonal cells were lesser in diabetics of over 10 years' duration when compared to diabetics of less than 10 years duration. (47)

Roszkowska et al studied corneal endothelium in both type I and type II diabetics. A total of 75 diabetics divided into type I and type II groups & 62 healthy individuals were included in the study. The mean central corneal thickness, endothelial cell density and morphology were measured and statistical analysis was performed. All the parameters that were evaluated showed a significant difference in both the diabetic groups with reduction in the mean endothelial cell density of 5% in type II diabetic group and of 11% in type I diabetic group when compared to the normal age-matched control group. Significant alterations in endothelial cell morphology were noted. The central corneal thickness was significantly more in diabetics, with $p < 0.01$ in type I diabetic group and $p < 0.05$ in type II diabetic group. This study concludes that corneal endothelium in diabetics should be regarded as a tissue under continuous metabolic stress with high vulnerability, mainly if there is any external insult such as surgical procedure. (6)

Busted et al captured corneal endothelium by specular microscopy in 81 insulin dependent juvenile diabetic patients and found minute folds in the corneal endothelial cell layer among 13 diabetics from the diabetic group and in 1 individual

among the normal group. There was no significant difference found in corneal endothelial cell density and dystrophic changes between diabetics and normal individuals. The increased corneal thickness in diabetics is deciphered as minimal corneal swelling. It presents very early in the disease and hence may be regarded as one of the earliest changes that can be clinically detectable in the diabetic eye. (48)

Calvo- Maroto et al compared 77 eyes of type 2 diabetics (33 males and 44 females) with 80 eyes of healthy individuals (42 males and 38 females) in the age group of 38 to 56 years. Central corneal thickness, corneal endothelial cell density (ECD), HbA1c levels, and Goldmann applanation tonometry were measured in all. It was observed that the CCT was remarkably higher and ECD was notably lower in long-term diabetics (10 years + since diagnosis) when compared to short-term diabetics (< 0.001). No significant differences were found in CCT ($p = 0.30$) and ECD ($p = 0.31$) between the control groups. (49)

Schultz et al conducted a study on corneas from 25 patients with type II diabetes mellitus for a duration of more than ten years by studying them under specular microscopy. And for comparison, 34 corneas from 21 age-matched nondiabetic individuals were examined. They also compared 31 corneas from 17 patients with type I (juvenile-onset) diabetes with 41 corneas from 23 age-matched normal volunteers. It was concluded from the study that corneal endothelium in type II diabetics showed no difference in endothelial cell density but showed a significantly higher coefficient of variation, decrease in the percentage of hexagonal cells & a low figure coefficient when compared to age matched nondiabetic individuals. Similar cell changes were noted in corneal endothelium with type I diabetes, but these changes were found in earlier decades itself. Moreover, they found a markedly higher rate of cell loss in type I diabetics leading to a significant decrease

in cell density in 4th& 5thdecades. These results clearly suggest that the corneal endothelium is morphologically abnormal in diabetics. (42)

Keoleian et al performed specular microscopy, anterior segment ocular fluorophotometry, corneal pachymetry and tonometry on 14 patients with chronic type I diabetes and non-proliferative retinopathy and compared these findings with those of 14 age-matched control subjects. It was concluded from the study that the eyes of diabetic patients showed an increase in the coefficient of variation of endothelial cell area, decrease in the percentage of hexagonal endothelial cells, raised IOP and increased corneal autofluorescence. Also, they found no difference in corneal thickness or endothelial cell permeability to fluorescein between the two groups. (50)

Storr Paulsen et al conducted a study to determine corneal endothelial cell density and morphology in type II diabetics and non-diabetics; to correlate potential differences to glycemic status. This prospective clinical study included 107patients with type II diabetes mellitus and 128 non-diabetics. More than 4 HbA1c tests were performed on diabetics (mean 4.1; range 2–14) at an interval of at least 3 months to reflect the long-term glycemic status. The parameters recorded were endothelial cell density, percentage of hexagonal cells, variation in endothelial cell size (CV) and central corneal thickness (CCT). No difference was found in corneal endothelial cell density, percentage of hexagonal cells and variation in cell size between Type II diabetics and normal subjects, but a significant increase in CCT (538 versus 546 microns, $p < 0.05$) was noted in diabetics when compared to normal subjects. Also, this study found that lower endothelial cell counts were associated with higher HbA1c levels ($p < 0.05$) in the diabetic group, but HbA1c did not have any impact on CCT. (2)

Sudhir et al conducted a population-based study to estimate the prevalence of type 2 diabetes mellitus and diabetic retinopathy in Chennai, South India by enrolling patients from the Sankara Nethralaya's Diabetic Retinopathy Epidemiology and Molecular Genetic Study. A total of 1191 cases and 121 controls were recruited into the study. In all the subjects, central corneal thickness was measured using ultrasound pachymeter and corneal endothelial morphological features were studied using noncontact specular microscopy. It was found that the mean corneal endothelial cell density was lesser in diabetics when compared to controls (2550 ± 326 vs. 2634 ± 256; P = 0.001). No difference was observed in the mean pachymetry values, percentage of hexagonality, and coefficient of variation of cell size between diabetics and controls. (51)

Studies on changes in corneal stroma:

It is hypothesized that few ion transport systems exist in the corneal endothelial cells to maintain the hydration and transparency of the corneal stroma. These ion transport systems mainly are Na+ - K + - ATPase, carbonic anhydrase and bicarbonate ions systems. The stroma imbibes water and swells up when the corneal epithelial and endothelial cell barrier is damaged, ultimately resulting in increased hydration of the corneal stroma and thickness. (30)

Studies on hyperglycemia induced biochemical processes in the cornea:

Hyperglycemia is regarded a vital factor in the pathogenesis of diabetes and several hyperglycemia-induced biochemical processes have been suggested. (52) One such biochemical process is elevated glucose to decreased Na+, K+-ATPase activity in the corneal endothelial cells. (53) Hyperglycemia causes intracellular accumulation

of sorbitol, an osmotic agent leading to the swelling of endothelial cells. This results in reduction in the endothelial pump function and ATP production. (46)

In vitro studies showed that polyhydroxy compounds like glucose, galactose, galactitol, sorbitol, or xylitol inhibit Na+, K+-ATPase activity in cultured bovine corneal endothelial cells, while in vivo studies showed reduced Na+, K+-ATPase activity in the corneal endothelial cells of diabetic rabbits after 10 weeks of alloxan-induced hyperglycemia.(54), (55) It was found that the diabetic rabbits had a higher baseline corneal thickness, decreased response of corneal swelling and slower recovery from hypoxic edema when compared to nondiabetic rabbits. This was not surprising as Na+, K+-ATPase is a major component of the endothelial fluid pump. (56)

Studies on long term corneal structural changes due to hyperglycemia:

Hyperglycemia associated with diabetes can cause increased protein glycosylation leading to increased production of advanced glycosylation end products (AGEs). (57) Studies show raised levels of AGEs in corneas of older diabetics. Increased AGEs in tissues causes increased collagen cross linking which results in gradual stiffening of corneal structure, ultimately leading to changes in corneal biomechanical properties. (58)

Abrupt correction of hyperglycemia in diabetics causes refractive changes in the eye, which can be attributed to changes in the morphology and function of the lens. **Zengin et al** proposed that hyperglycemia affects not only the corneal hydration, but also the qualitative and quantitative corneal changes such as refractive index, corneal curvature and thickness. (59-61)

Studies on corneal biomechanical changes in diabetics:

The idea about the viscosity of the cornea is given by corneal hysteresis. Therefore, it reflects changes in the organization of corneal stromal collagen, whereas corneal resistance factor is associated with stiffness of cornea.

Kotecha et al performed a study on corneal thickness and age-related biomechanical properties of the cornea using Ocular Response Analyzer. This instrument, Ocular Response Analyzer (ORA) measures the corneal hysteresis (CH) to rapid indentation by an air jet. The difference in applanation pressures (P1, P2) between the rising phase and falling phase of the air jet is CH.

They performed a characterization study and a validation study. The purpose of characterization study was to analyze the intraocular pressure (IOP)–dependence of CH and to characterize the performance of ORA. The purpose of validation study was to evaluate association between CH and both age and central corneal thickness (CCT).

"For the characterization study, data were collected from 105 untreated subjects (45 ocular hypertensive patients and 60 normal subjects; mean age, 60 years, range, 26– 82). GAT and ORA measurements were performed before and after IOP lowering of 32 one randomly selected eye with apraclonidine drops. The change in P1 and P2 (arbitrary units) in relation to change in GAT IOP was analyzed to calibrate the instrument. The relation between P1, P2, and CCT was explored and ORA IOP was derived from the analyses. For the validation study, ORA and GAT IOP and CCT were measured in 144 eyes of 144 untreated subjects (mean age, 58 years; range, 19 – 83). The characterization calculations were applied to the dataset and values of CH

and ORA IOP were calculated. The relationship between CH and both subject age and CCT was determined. The associations between CH and CCT and between ORA and GAT IOPs, were investigated by linear regression analysis. The agreement between measuring devices was calculated. In the characterization study, P1 changed by 6.41 arbitrary units for every 1-mm Hg change in GAT IOP. CH (P1 − P2) changed by −1.60 arbitrary units for every 1-mm Hg change in GAT IOP. For each unit change in P2, P1 changed by 1.27 units. From this association a new IOP-independent corneal factor was derived [P1 − (P2/1.27)] and is termed the corneal constant factor (CCF; mm Hg). ORA IOP normalized for CCF was defined as P2 – CCF (mm Hg). The CCF (mm Hg) was associated with CCT (micrometers) and with age: CCF = [(0.036 · CCT) − (0.028 · age)] + 1.06 (adjusted r 2 = 0.34; P < 0.0001 for CCT, P = 0.007 for age). Normalized ORA IOP measurements were not associated with CCT. GAT IOP was associated with CCT and CCF—more strongly with the latter: GAT IOP = (0.03 · CCT) +1.52 (r 2 = 0.06, P = 0.002); GAT IOP = (0.65 · CCF) + 4.5 (r 2 = 0.13, P < 0.0001). The mean difference (95% limits of agreement) between GAT and normalized ORA IOP was 0.1 (−6.6 to +6.8) mm Hg. The CCF describes an IOP independent biomechanical property of the cornea that increases with thicker CCT and decreases with greater age. It is moderately strongly associated with CCT and yet explains more of the interindividual variation in GAT IOP than does CCT. Normalized ORA IOP measurements are not associated with CCT." [62]

Scheler et al performed a study on 35 healthy individuals and 31diabetics to find out whether corneal resistance factor (CRF) and corneal hysteresis (CH) are affected in diabetics and to know whether these parameters are related to HbA1c. Diabetics were divided into 2 groups, group 1 with HbA1c <7% (n = 14) and group 2 with HbA1c >7% (n = 17). CH and CRF were evaluated by using ocular

response analyzer (ORA). It was found that CH and CRF are significantly higher in uncontrolled diabetics when compared to healthy individuals and well-controlled diabetics. And they observed a correlation of CH and CRF with HbA1c, which suggests that the biomechanical properties of cornea change based on glycemic control. (56)

Yazgan et al measured biomechanical parameters of cornea by using ocular response analyzer in 156 diabetics and 74 healthy individuals. Subjects were categorized into 3 groups: Group 1 consisted of healthy control subjects, Group 2 with diabetics having HbA1C <7% and Group 3 with diabetics having HbA1C ≥7%. It was found that corneal biomechanical properties were affected in both the diabetic groups when compared to healthy subjects. (57)

According to **Herse et al**, abnormal corneal hydration in diabetics causes increased corneal thickness and altered corneal endothelial morphology. In this study, the influence of hyperglycemia on corneal hydration control was evaluated by experimenting on normal and alloxan-induced diabetic rabbits. The parameters assessed in the study were:

(1) stromal dry weight, hydration& swelling pressure
(2) corneal thickness & contact lens-induced edema recovery responses
(3) activity of endothelial homogenate sodium/potassium adenosine triphosphatase (Na+/K+ ATPase)

The study revealed that uncontrolled hyperglycemia in the rabbit for 10 weeks resulted in abnormal corneal hydration control, which was suggested by increased corneal thickness, increased stromal hydration& decreased capability to recover from contact lens induced corneal edema. No significant difference was noted between swelling pressures and dry weights of the normal and diabetic stroma. Reduction in

the activity of endothelial homogenate Na+/K+ ATPase in diabetic rabbit strongly indicates that dysfunction of the endothelial fluid pump is a major component in abnormal corneal hydration control. (54)

Studies on corneal metabolic and permeability changes in diabetics:

Keoleian et al performed specular microscopy, anterior segment ocular fluorophotometry, corneal pachymetry and tonometry on 14 patients with chronic type I diabetes and non-proliferative retinopathy and compared these findings with those of 14 age-matched control subjects. It was concluded from the study that the eyes of diabetic patients showed an increase in the coefficient of variation of endothelial cell area, decrease in the percentage of hexagonal endothelial cells, raised IOP and increased corneal autofluorescence. Also, they found no difference in corneal thickness or endothelial cell permeability to fluorescein between the two groups. Therefore, despite the structural abnormality in the endothelial cells, they were unable to find any abnormality in endothelial cell function in diabetic corneas in the unstressed state. (50)

Larsson et al conducted a study by enrolling 49 patients with type I diabetes mellitus and 60 patients with type II diabetes mellitus from Mayo Clinic, Rochester, Minn. 31 normal subjects were taken as controls. Using fluorophotometry, corneal endothelial permeability and corneal autofluorescence were evaluated. It was found that there was no difference in endothelial permeability and cell density between both type I & type II diabetic and control groups. Pleomorphism, polymegathism, increased corneal thickness& autofluorescence were noted in type 1 diabetics when compared to controls. The severity of diabetic retinopathy was markedly correlated only with corneal autofluorescence. The corneas of type I diabetics showed

abnormalities in the morphology of endothelial cell characteristics & corneal autofluorescence. No abnormalities were found in the corneal endothelial cell permeability in both type I &type II diabetics. [63]

Central Corneal thickness (CCT) in diabetics

Central corneal thickness was evaluated in diabetics in various studies. [9], [64-69]. CCT is an important variable which affects IOP & is also an independent risk factor for glaucoma. IOP is overestimated by thick CCT and underestimated thin CCT. [70]

Central corneal thickness in normal eyes:

Normal corneal thickness varies from central to peripheral limbus. It ranges from 0.7 to 0.9 mm at the limbus and 0.49 mm to 0.56 mm at the centre. The Central corneal thickness (CCT) value of more than or equal to 0.7 mm is suggestive of endothelial decompensation. According to various studies, mean CCT is 0.51-0.52 mm. Due to age-related anatomic changes, it was found that cornea is markedly thicker in the age group of 40 – 80 years when compared to individuals below 40 years. Peripheral corneal thickness is asymmetric; thinnest is temporal cornea followed by the inferior cornea.

Factors affecting central corneal thickness:

- CCT is higher in young, males& diabetics.
- No correlation with refraction or systemic hypertension.
- Mean CCT of black children is thinner when compared to white children.
- African-Americans have thinner corneas when compared to whites.
- PITX2/Pitx2 mutation occurring in Axenfeld-Rieger malformations leads to decreased corneal thickness.

Role in clinical practice:

1) **Glaucoma:** for applying correction factor to determine actual intraocular pressure (IOP).

2) **Congenital Glaucoma:** to evaluate the amount of corneal edema.

3) **Refractive surgeries:**

a) for screening preoperatively

b) to plan treatment for keratorefractive procedures like LASIK, astigmatic keratotomy and earlier even prior to radial keratotomy.

4) Postoperative follow up in patients who undergo keratoplasty to determine endothelial cell function.

5) **Contact lens:** in orthokeratology and to assess corneal edema.

6) To assess the thinness of corneas in corneal disorders such as Terrien's and Pellucid marginal degenerations, keratoconus, keratoglobus & post LASIK ectasia.

Correction factor: It is recommended that in chronic eye diseases like glaucoma and glaucoma suspects for every 50 microns rise in CCT, the recorded IOP should be decreased by 2.5mm Hg.

Methods of Measurements

1. Ultrasonic techniques

a. Conventional ultrasonic pachymetry

b. Ultrasound Bio microscopy (UBM)

2. Optical Techniques

a. Manual Optical Pachymetry

b. Specular Microscopy

c. Scanning Slit Technology

d. Optical Coherence Tomography (OCT)

e. Optical Low Coherence Interferometry

f. Confocal Microscopy

g. Laser Doppler interferometry

3. Alternative Measurements

a. Pentacam

b. Pachycam

c. Ocular response analyzer (ORA)

Ultrasonic Pachymetry

This is the most commonly used and gold standard method these days. The ultrasonic pachymeter was introduced by Henderson and Kremerin 1980.

Principle

The ultrasonic pachymetry measurements depend on the reflection of ultrasonic waves from the anterior and posterior corneal surfaces. The time difference (transit time) between echoes of ultrasonic signal pulses from the transducer of the probe and the reflected signal from the front and back surface of the cornea to the transducer is measured.

Corneal thickness is calculated by following simple formula:

Corneal thickness = (Transit time × Propagation velocity) / 2

The velocity of sound through normal cornea is taken as 1640 m / sec.

Components:

There are 3 main components in Ultrasonic pachymeter

a. Probe handle It has a piezoelectric crystal that vibrates at 10 - 20 MHz It is a hand-held probe that is very small, light and easy to use.

b. Transducer It sends ultrasound rays to the cornea through the probe & receives echoes from cornea.

c. Probe tip Diameter of the probe tip should not be > 2 mm, so that the area where the tip of the probe is kept can be seen and also ultrasound beam spreads over a lesser area. The tip of the probe tip should be smooth so that damage to the corneal epithelium can be avoided. While performing, the probe tip should be placed perpendicular to the centre of cornea. Lateral displacement of the probe shows elevated readings as the corneal thickness increases peripherally.

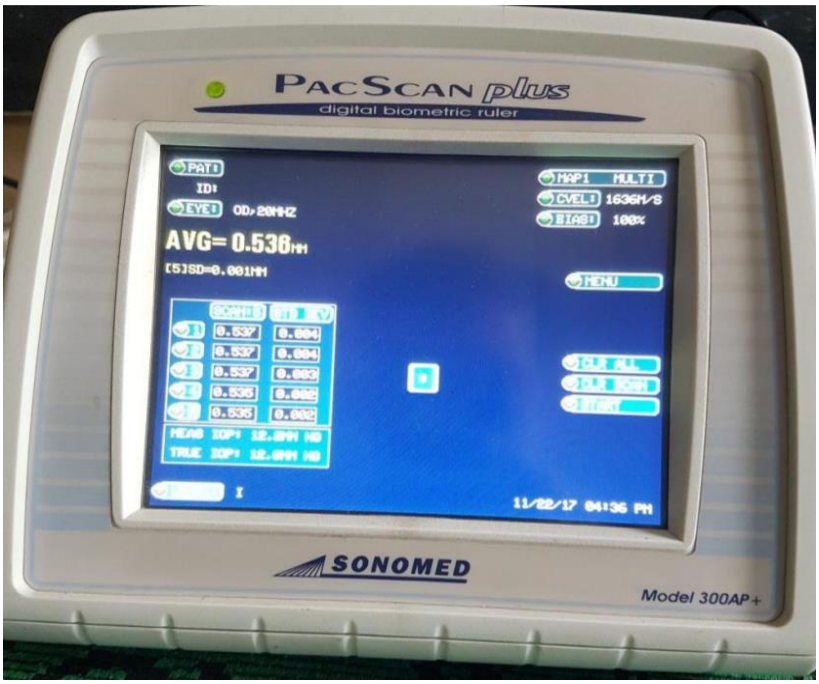


Fig 3: Ultrasonic pachymetry

Advantages

- Simpler & fast, hence easier for the paramedical staff to use
- Minimal observer judgement is needed, so it is consistent and repeatable between observers and hence interobserver variation can be eliminated.
- Portable
- No coupling agent is required
- Can be used intraoperatively

Disadvantages

- Contact method
- Accuracy depends on perpendicular application of the probe on the cornea
- Reproducibility depends on precise placement of the probe on the centre of the cornea.
- Difficult to control the patients gaze during repeated measurements.

- Speed of the sound becomes variable depending on whether the tissue is wet or dry.
- Resolution is low
- Inaccurate in oedematous corneas

Ultrasound Bio microscopy (UBM)

It (Paradigm Med Ind, Inc. Salt Lake City, UT) is a high-resolution ultrasound machine which captures the anterior segment of eye. It has a 12.5 - 50 MHz probe, whose depth of penetration is lesser (4 mm) than the conventional and it gives real-time images. Corneal thickness is analysed with the help of a caliper, that is incorporated in the machine or with the UBM software after acquiring images.

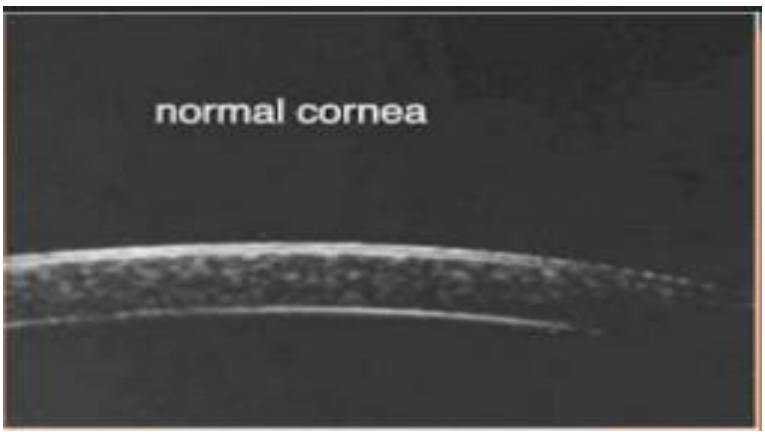


Fig 4 : UBM showing normal cornea with two smooth highly reflective surface echoes from epithelial surface and bowman's membrane. Stroma shows low reflectivity. Descemet's membrane / endothelial surface has smooth highly reflective line

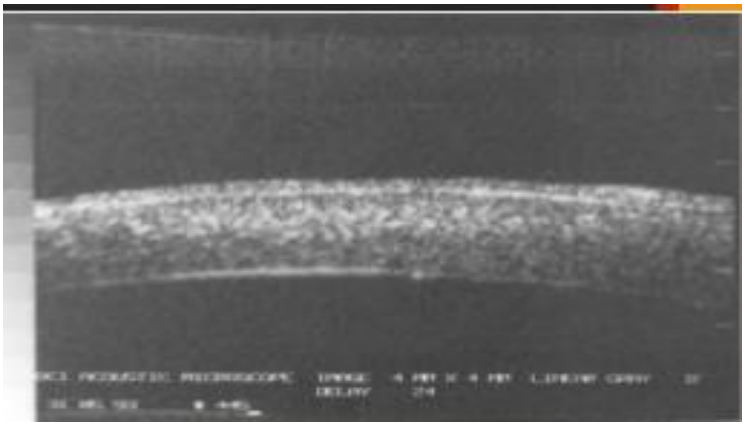


Fig 5: UBM showing edematous cornea. Epithelium is thickened and irregular. Stroma is thickened and shows increased reflectivity.

Advantages:

- Along with corneal thickness, anterior segment examination (high resolution) can also be carried out.
- Useful in opaque corneas.
- Layers of cornea can be made out.

Disadvantages:

- The main disadvantage is that, it requires immersing of the eye in a coupling fluid.
- Contact method.
- Patient is required to lie supine during the examination
- Machine cannot be used intraoperatively.
- Standardization is difficult.

Manual optical pachymetry

Central corneal thickness is measured using Haag-Streit slit lamp using the pachymeter attachment (Haag Streit AG, Koeniz, Switzerland). It is the prototype of optical pachymeter. Through the narrow diaphragm of the instrument, a slit beam is

projected perpendicularly onto the cornea. It comes with or without a Mishima-Hedbys fixation attachment to ensure the perpendicularity of the incident beam. The instrument consists of 2plano glass plates that split the image of the corneal parallelepiped. The regular eyepiece of the slit-lamp is replaced by uniocular right-sided split-image eyepiece.

Methods to measure corneal thickness:

"Just touch" method:

The observer moves the instrument scale until the focused upper half of the corneal image is positioned so that its posterior surface (endothelial border) just touches the anterior surface (epithelial border) of the lower image. This method is easier and more practical.

"Overlap method":

The bright line of endothelial border overlaps with bright line of epithelial border. From the scale on the instrument, the corneal thickness is then directly read. The range of measurement is from 0 to 1.2 mm, with a least gradation of 0.02 mm.

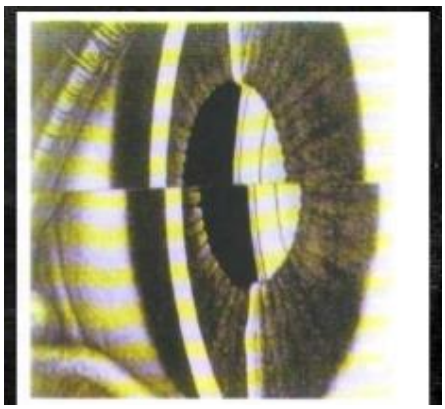


Fig 6: Manual optical pachymetry

Disadvantages:

- Lack of accuracy. It is found that the accuracy of optical pachymeter values using the Haag-Streit attachment can be increased by correcting for the corneal curvature. Usual range of error with an optical pachymeter is ± 2%.
- Lack of repeatability, which is due to fixed position of the fixation target. Moreover, the end point is subjected to observers' bias and the width of slit lamp beam lacks compensation.
- Requires slit lamp and hence has poor portability and so, cannot be used in operating room.

Specular pachymetry

It is the oldest method to evaluate corneal thickness.

Principle:

The distance between the anterior and the posterior surfaces of cornea is measured and depends on the light rays focusing through front and back of cornea.

Types:

1. Contact

2. Non-contact

The newer non-contact machines are better because they do not touch the cornea. They are quick and easy & also equipped with auto-focus and image analysis program. But readings measured by non-contact method are found to be significantly thinner than contact method.

Advantages

- Operator independent
- Non invasive
- Simultaneous cell count measurement

Disadvantages

- Exact point where the reading is taken cannot be known.
- Risk of infection and epithelial damage with contact method.
- Time consuming.
- Less reproducibility.
- Cannot be used in operation room
- Clinical use is limited to corneas free of edema, scarring, deposits or opacities that may distort light transmission.

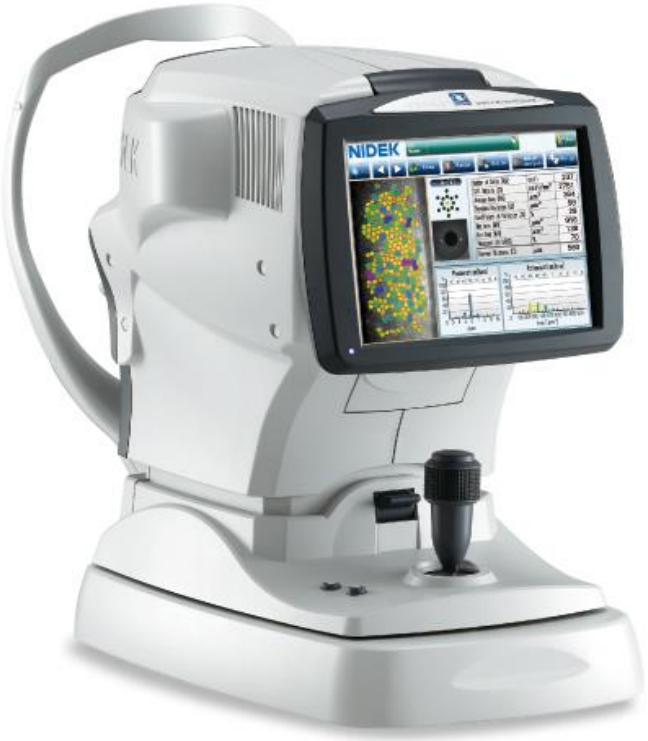


Fig 7: Specular microscopy

Slit-scanning pachymetry

The Orbscan II (Bausch & Lomb, Rochester, NY, USA) uses scanning slit technology. It assesses multiple functions of the cornea, thickness, anterior and posterior topography, elevation& anterior chamber depth. It gives pictorial representation of corneal topography in the form of 4-coin map.

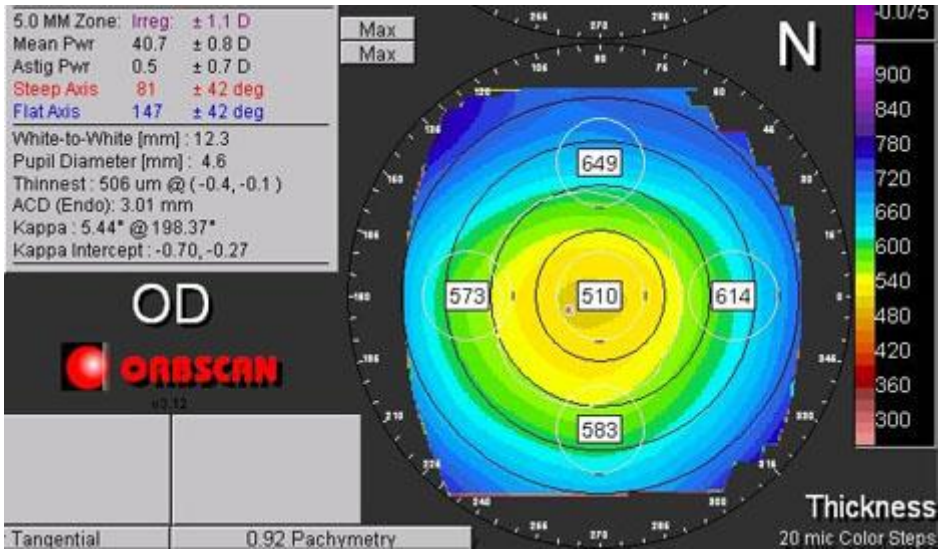


Fig 8: Orbscan

Principle:

By comparing to a best fit sphere, it measures anterior and posterior corneal elevations and the difference between elevation of anterior and posterior corneal surface is calculated.

Advantages

- Wide field pachymetry.
- Thinnest point of the cornea can be identified both by value and location. In a normal eye, thinnest point is very near to the geometric centre of the cornea. If the thinnest point is off centre, then it is suggestive of corneal health problems like keratoconus.

- Corneal alignment is not required.
- Used to calculate ablation depth & optical zones in corneal refractive surgeries.

Disadvantages

- The main drawback of Orbscan is that corneal thickness is underestimated in Keratoconus, post-PRK, and post-LASIK eyes due to the following reasons:
- Scattering from corneal haze and stromal interface, which interferes with the identification of the corneal surface reflections.
- The measurements are adjusted for normal prolate shape of cornea. If there's a change in shape, that interferes with the reconstruction algorithms.
- It has got importance in refractive surgery. The amount of residual bed that is to be left should be greater if pachymetry is done with Orbscan than with conventional ultrasound. On an average, it is 28 microns higher with the Orbscan than with the ultrasound pachymeter in normal eyes & 13 micron lower in post-LASIK eyes.
- Not fast enough for the pachymetry mapping due to motion artifacts.
- When clinically significant haze is present, Orbscan system shows decreased accuracy in measuring corneal thickness.

Anterior Segment Optical Coherence Tomography (ASOCT)

ASOCT (Visante-Carl Zeiss Meditec AG) is a high resolution, non- contact optical coherence tomography specialized for anterior segment. It gives high resolution corneal images. It provides color coded map of the corneal thickness.

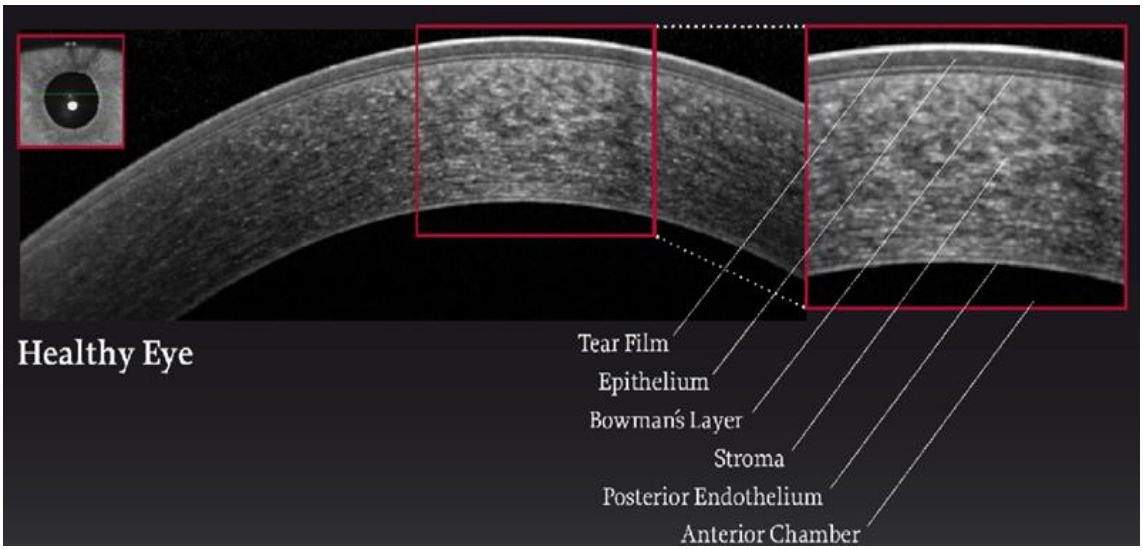


Fig 9: Anterior segment optical coherence tomography

Advantages

- Noncontact
- accurate and repeatable
- High Resolution
- It measures and documents both corneal flap thickness & residual stromal thickness immediately following LASIK surgery.
- Can measure through corneal opacity

Optical Low Coherence Reflectometry (The Haag-Streit OLCR)

This device is attached to a slit lamp & is a single mode fiberoptic based Michelson's interferometer that has a high repetition rate. It can measure corneal thickness to a precision of one micron.

Principle:

It is based on Michelson interferometer. Diode laser beam is used here. Due to the differences in refractive index occurring at air-to-cornea &cornea-to-anterior chamber interfaces, the measurement beam is reflected from anterior & posterior corneal surfaces. These reflections reach the detector back. The interference signals are generated when the light emitting diode (LED) beam strikes the front and back surfaces of the cornea perpendicularly. It comes in 2 forms:

1. Slit lamp mounted

2. Excimer laser mounted

Advantages:

- Precise.
- Automatic alignment.
- Non-contact.
- Real-time data acquisition and display.
- Convenient and easy.
- Variability of measurements is significantly lower than the measurements taken with the contact ultrasound pachymetry.
- Intraoperative measurements possible.

Disadvantages:

- Only central corneal thickness can be measured.

Confocal Microscopy

The focus of the objective lens in the Z-axis or rapid movement of the objective lens itself is automated and registered by a computer. The amount of light that is backscattered by the central section of each image is recorded in order to allow an intensity profile curve to be generated.

Advantages:

1. For measuring thin layers such as epithelial or Bowman's layer thickness, it offers moderate to good repeatability.

2. Flap thickness can also be obtained following laser in situ keratomileusis (LASIK) surgery.

3. z-scan curve is used to assess the level and location of corneal haze associated with the various corneal dystrophies.

Disadvantages:

- The precision of measurements will vary with this technique with contact lens hydration, post-lens tear film thickness and observation angle.
- Data acquisition is slower
- Poor penetration of corneal opacity
- Cumbersome

Pentacam

It evaluates complete anterior segment, corneal topography, anterior chamber, angle measurements, quantification of lens density& utility to monitor new therapeutic modalities like collagen crosslinking treatment for keratoconus.

Principle:

Pentacam (Oculus Inc., Germany) is based on evaluation of true elevation and captures the anterior segment (cornea + lens) of the eye by a rotating Scheimpflug camera measurement which supplies images in 3 dimensions. The corneal centre is measured very accurately because of this rotational imaging process. The corneal thickness is shown as a color image, showing the total area from limbus to limbus.

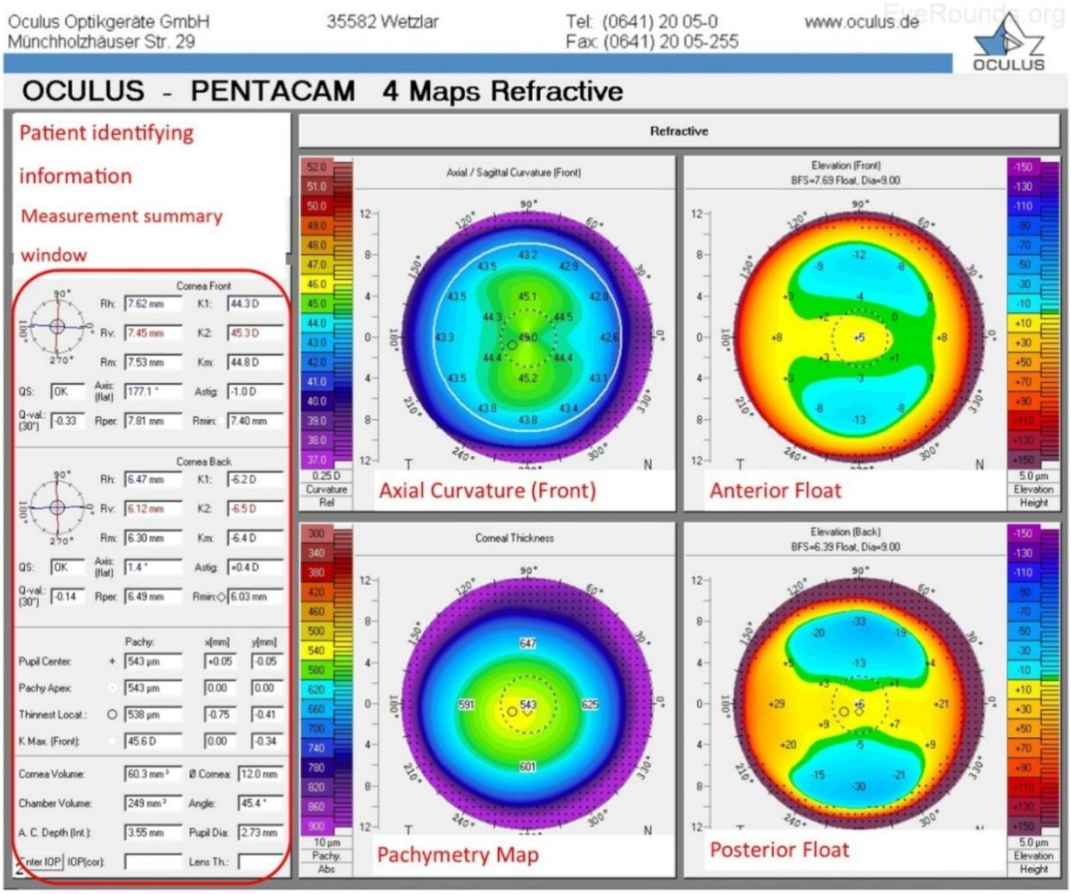


Fig 10: Pentacam

Advantages:

- Non-invasive, noncontact
- Even minute ocular movements are captured & corrected simultaneously.
- precise representation and repeatability.
- The high quality of the Scheimpflug image allows pre and postoperative monitoring as in the case of an intraocular contact lens.

Disadvantages

- It underestimates the corneal thickness when compared to ultrasonic pachymetry.

Pachycam

The Oculus Pachycam is a compact and portable noncontact pachymeter which has a built-in keratometer. It can be mounted on a slit lamp. It corrects the IOP automatically in accordance with correction tables to obtain the "real" IOP. Image is taken with the help of a 3D alignment screen.

Principle:

Scheimpflug principle of the horizontal 4 mm cut image which is evaluated and represented. It also gives central k-values as well as the local k-readings on the 4 mm cut.

Advantages:

1. Noncontact
2. Immediate indication of central and thinnest pachymetry readings
3. Compact, portable, light weight

Ocular response analyzer

Newer modality for measuring biomechanical properties of eye. It measures corneal hysteresis. [72]

TABLE 7-1. COMPARISON OF PACHYMETRY METHODS

Method	Traditional Ultrasound	Ultrasound Biomicroscopy and Very-High-Frequency Ultrasound	Optical Slit-Lamp Pachymetry	Specular Microscopy Based: Contact and Noncontact	Scanning-Slit Based: Orbscan	Optical Coherence Tomography	Optical Low-Coherence Reflectometry	Confocal Microscopy Through-Focusing	Laser Doppler Interferometry
Operating principle	10- to 20-MHz frequency sound waves	50-MHz (ultrasound biomicroscopy) and 70-MHz sound waves	Image doubling, manual	Measures focus through front-back cornea	Scanning-slit: front-back corneal reflections	Infrared interferometry	Infrared interferometry (like OCT)	Focuses through planes with a confocal microscope	Dual-beam laser Doppler
Contact/ noncontact	Contact	Contact with water bath	Noncontact	Both contact and noncontact	Noncontact	Noncontact	Noncontact	Contact	Noncontact
Resolution	No sublayer pachymetry	Sublayer pachymetry	No sublayer pachymetry	No sublayer pachymetry	No sublayer pachymetry	Sublayer pachymetry	Potential for sublayer pachymetry	High resolution with sublayer pachymetry and cellular details	No sublayer details
Dimensional sections (2D/3D)	Low resolution, NA	High-resolution 3D views possible	No	No	2D display of data	2D display of data	Not available, potential possible	3D views	No
Peripheral pachymetry	Not reliable	Easy to obtain, difficult to standardize	Not reliable	Not reliable	Standard	Easy to obtain, relatively easy to standardize	Not available, potential possible	Requires repositioning	Not reliable
Special applications	Most common method used clinically	Postrefractive surgery: lamellar thickness	Slit-lamp mounted	Simultaneous measurement of cell counts	Postrefractive surgery	Postrefractive surgery	Intraoperative measurement during laser ablations	Cellular morphology/ detail; detects microbes	Can measure axial length
Advantages	Fast, simple, dry technique	Sublayer detail	Simple	Measure cell counts concurrently	Concurrent topography/ elevation data	Measures through opacity, high resolution	Intraoperative measurements possible	High resolution, can quantify haze/light scatter	Purportedly good precision
Disadvantages	Not accurate in edematous corneas, difficult to reposition/ standardize location with precision	Requires water bath, risk of corneal abrasion, complicated technique, difficult location standardization	Manual: observer-dependent precision	Contact method: risk for abrasion of corneas	May be less accurate post-laser *in situ* keratomileusis or in corneas with haze	Interinstrument variability, preliminary clinical experience to date	Currently not able to acquire 2D or 3D images, same as for OCT	Slow data acquisition, poor penetration of corneal opacity, contact method, minimal clinical experience	Minimal clinical experience reported to date

Table 1: Comparison of pachymetry methods

CCT in various populations:

Studies which have measured CCT from different populations without any corneal pathology provide guidance. Mean CCT for specific populations lie between 510 - 560 microns with majority being closer to 530-550 microns. Thinnest mean CCT is reported in central/southern Indians [73], [74], Japanese, Australian Aborigines, North and west Africans, African Americans. The thickest mean CCT is found in European, White American and Latino populations. [75-85]

MATERIALS AND METHODS

This is a cross-sectional study carried out during the period of April 2018 – October 2020 on the patients attending the inpatient as well as outpatient department of Ophthalmology, B.L.D.E. U's Shri B.M. Patil Medical College, Hospital and Research Centre, Vijayapura. The study includes 168 adult subjects divided into three groups:

a. 46 patients with Type 2 Diabetes Mellitus for a duration less than or equal to 10 years

b. 40 patients with Type 2 Diabetes Mellitus for a duration more than 10 years

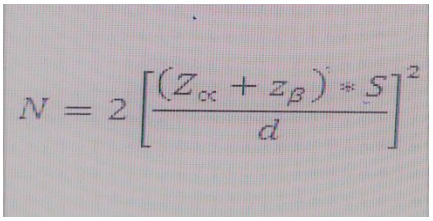
c. 82 controls who were randomly selected from the patients visiting Ophthalmology department.

The patients were explained about the study and patients' willful consent was taken. Details of the patients including history, clinical examination, investigations were recorded. Clinical examination includes visual acuity (by Snellen's chart), slit lamp examination, dry and cycloplegic (if required) retinoscopy with streak retinoscope and subjective correction. Pachymetry and intraocular pressure (by applanation tonometry) were recorded.

Central corneal thickness was measured using a hand held ultrasonic pachymetry (PAC Scan plus, model: 300 AP+, Sonomed). The corneas of both the eyes were anesthetized with topical anaesthetic eye drops 0.5% Proparacaine and central corneal thickness readings were taken after 90 seconds of instillation. The patient was seated and asked to fixate at a target in the front. The pachymetry probe is brought in light contact with the cornea centrally and perpendicularly and five readings on each side are taken. Central corneal thickness was taken as the average of

those five readings. On the basis of a study the anticipated Mean ±SD of central corneal thickness in Diabetics was 564±30 and central corneal thickness in non-diabetics was 538±35[9]. With the mean difference of thickness and common standard deviation, the minimum sample size is 40 per group with 95% level of significance and 90% power.

Formula used is



$$N = 2\left[\frac{(Z_{\alpha} + z_{\beta}) * S}{d}\right]^2$$

Calculated sample size per group = 40

Total sample size taken in the study is 168

Diabetes for duration < or equal to 10 years N1 = 46

Diabetes for duration >10 years N2 = 40

Total study population = 86

Non-diabetics N3 = 82

Total sample size = 168

STATISTICAL TOOLS USED FOR DATA ANALYSIS AND RESULTS TABLES ARE EVOLVED THROUGH DATA ANALYSIS TOOL IN MS-EXCEL AS AN ADD ON TOOL

THEORITICAL CONCEPTS AND EQUATIONS

COVARIANCE:

- It is s systematic relationship between a pair of random variables wherein a change in one variable reciprocated by an equivalent change in another variable.

- It can take any value between -∞ to +∞, wherein the negative value is an indicator of negative relationship whereas a positive value represents the positive relationship and when the value is zero, it indicates no relationship.
- Calculation of Covariance:
- For the set of 'n' units of observations be given by the ordered pairs (x_1, y_1), (x_2, y_2) ……. (x_n, y_n), where n is the number of sets or observations.

  Calculate $\bar{x} = (x_1+x_2+\ldots\ldots\ldots+x_n)/n$ or $(\sum_{i=1}^{n} x_i)/n$

  Calculate $\bar{y} = (y_1+y_2+\ldots\ldots+y_n)/n$ or $(\sum_{i=1}^{n} y_i)/n$

Calculate: $\sum_{i=1}^{n}(x_i - \bar{X})(y_i - \bar{y})$

Covariance: $(X, Y) = \dfrac{\sum_{i=1}^{n}(x_i - X)(y_i - y)}{n}$

Correlation:

- A measure which determines the change in one variable due to change in another variable.
- Correlation can take any value between -1 to +1, wherein values close to +1 represents strong positive correlation and values close to -1 is an indicator of strong negative correlation.

$$\text{Correlation } (X, Y) = \frac{\dfrac{\sum_{i=1}^{n}(x_i - X)(y_i - y)}{n}}{\sqrt{\text{Variance of X} * \text{ Variance of Y}}}$$

ANALYSIS OF VARIANCE (ANOVA):

Analysis of variance is a collection of statistical models and their associated estimation procedures used to analyse the differences among group means in a sample. There are two types i.e. one-way anova and two-way anova.

a) <u>Calculation of Variance Between the Samples:</u>

It is the sum of the squares of the deviations of the means of various samples.

(i) Calculate the sample means $\overline{X_1}, \overline{X_2}$…….$\overline{X_k}$ of k samples.

(ii) Calculate mean for it i.e. $\frac{\overline{X_1} + \overline{X_2}\ldots\ldots\overline{X_k}}{K}$ = T/ N where

T= grand total of all observations and N = total No.of observations in K samples.

Calculate find. $\overline{X_1} - \overline{X},\ \overline{X_2} - \overline{X}, \ldots\ldots\ldots\overline{X_k} - \overline{X},$

Calculate: SSB (or SSC) = Sum of the Squares of the variations between the samples (or between the columns)

$= \sum_{i=1}^{k} n_I\ (\overline{X_i} - \overline{X}\ )^2$

Calculate: MSB (Or MSC) = variance or the Mean Square Between the samples (or between the columns)

= SSB / (K-1) where K = No. of samples

(a) Calculations of Variance within the samples:

It is the sum of the squares of the deviations of the means of various samples.

(i) Calculate the sample means $\overline{X_1}, \overline{X_2}$…….$\overline{X_k}$ of k samples.

(ii) Calculate the deviations of various k samples from mean values and Square these deviations and obtain their total

Calculate: SSW = Sum of the squares of the variations within the samples.

$$\sum (X_1 - \overline{X_1})^2 + \sum (X_2 - \overline{X_2})^2 + \cdots\cdots\cdots\cdots \sum (X_K - \overline{X_K})^2$$

Calculate: MSW = SSW / N-k Where N= Total No. of observations and K =No. of samples

(C) **Calculation of the Test Statistic F**

Assuming that H_o is true, the Test Statistic

F = MSB / MSW = Variance between the samples / Variations within the samples with degrees of

freedom k -1 and N-k

ANOVA TABLE (ONE – WAY CLASSIFICATION)				
Source of variation (SV)	Sum of Squares (SS)	Degrees of freedom	Mean Squares (MS)	Test Statistic (F- Ratio of variance)
Between samples (Columns)	SSB	k-1	MSB =SSB/k-1	
Within samples (Errors)	SSW	N-k	MSW = SSW / N-k	F = MSB / MSW
Total	SST	N-1	--	--

SST = SSB + SSW = Total sum of squares of variations.

Table 2: ANOVA table (one – way classification)

CONCEPT OF P –VALUE: The p-value is calculated using the sampling distribution of test statistic under Null Hypothesis, the sample data, type of test being done.

What Is P-Value?

In statistics, the p-value is the probability of obtaining results as extreme as the observed results of a statistical hypothesis test, assuming that the null hypothesis is correct. The p-value is used as an alternative to rejection points to provide the smallest level of significance at which the null hypothesis would be rejected. A smaller p-value means that there is stronger evidence in favour of the alternative hypothesis.

How Is P-Value Calculated?

P-values are calculated using p-value tables or spreadsheets/statistical software. Because different researchers use different levels of significance when examining a question, a reader may sometimes have difficulty comparing results from two different tests. P-values provide a solution to this problem.

For example, if a study comparing returns from two particular assets were undertaken using by different researchers who used the same data but different significance levels, the researchers might come to opposite conclusions regarding whether the assets differ.

To avoid this problem, the researchers could report the p-value of the hypothesis test and allow the reader to interpret the statistical significance themselves. This is called a p-value approach to hypothesis testing.

P-Value Approach to Hypothesis Testing

The p-value approach to hypothesis testing uses the calculated probability to determine whether there is evidence to reject the null hypothesis. The null hypothesis, also known as the conjecture, is the initial claim about a population (or data generating process).

The alternative hypothesis states whether the population parameter differs from the value of the population parameter stated in the conjecture.

In practice, the significance level is stated in advance to determine how the small the p-value must be in order to reject the null hypothesis.

Type I Error

A type I error is a false rejection of the null hypothesis. This occurs when the null hypothesis is true in reality, but the null hypothesis is rejected, having a p-value that is less than the significance level (often 0.05). The probability of a type I error is the significance level (again, often 0.05), and is the relative frequency of occurrence of obtaining a p-value that is less than the significance level, assuming the null hypothesis is true.

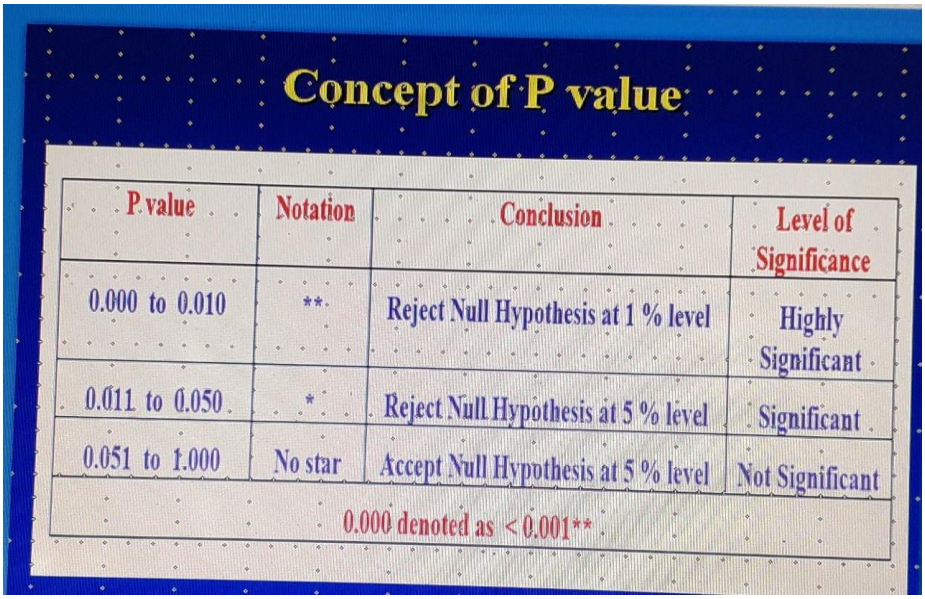
Real-World Example of P-Value

Assume an investor claims that their investment portfolio's performance is equivalent to that of the Standard & Poor's (S&P) 500 Index. To determine this, the investor conducts a two-tailed test. The null hypothesis states that the portfolio's returns are

equivalent to the S&P 500's returns over a specified period, while the alternative hypothesis states that the portfolio's returns and the S&P 500's returns are not equivalent. (If the investor conducted a one-tailed test, the alternative hypothesis would state that the portfolio's returns are either less than or greater than the S&P 500's returns.)

One commonly used significance level is 0.05. If the investor finds that the p-value is less than 0.05, then there is evidence against the null hypothesis. As a result, the investor would reject the null hypothesis and accept the alternative hypothesis. The smaller the p-value, the greater the evidence against the null hypothesis. Thus, if the investor finds that the p-value is 0.001, there is strong evidence against the null hypothesis, and the investor can confidently conclude the portfolio's returns and the S&P 500's returns are not be equivalent.

Conversely, a p-value that is greater than 0.05 indicates that there is (at best) weak evidence against the conjecture, so the investor would fail to reject the null hypothesis. In this case, the differences observed between the investment portfolio data and the S&P 500 data are explainable by chance alone.



Concept of P value

P value	Notation	Conclusion	Level of Significance
0.000 to 0.010	**	Reject Null Hypothesis at 1 % level	Highly Significant
0.011 to 0.050	*	Reject Null Hypothesis at 5 % level	Significant
0.051 to 1.000	No star	Accept Null Hypothesis at 5 % level	Not Significant
0.000 denoted as < 0.001**			

Table 3: Concept of P value

INCLUSION CRITERIA:

a. Patients with type 2 diabetes mellitus above 30 years of age
b. Glycosylated Hb $\leq$ 7.2%

EXCLUSION CRITERIA:

a. Patients who had already undergone intraocular or corneal surgery
b. Patients previously diagnosed with any corneal pathology
c. Patients who had worn rigid contact lens during the month prior to ophthalmic examination
d. Patients who had worn soft contact lenses seven days before ophthalmic examination
e. Raised IOP.
f. Hypertension
g. Diabetics with neuropathy or nephropathy

RESULTS

Comparison of CCT between diabetics and non-diabetics

CCT(NOND)		CCT(D)	
RE (NOND)	**LE (NOND)**	**RE (D)**	**LE (D)**
502	510	524	523
483	499	501	504
524	518	519	522
532	530	544	542
514	518	536	530
478	480	529	531
507	505	521	523
525	522	535	539
540	542	520	519
512	514	525	527
503	502	504	508
494	501	523	526
528	525	539	537
511	509	526	521
484	501	530	530
533	531	531	531
510	522	568	571
531	532	555	558
502	503	526	525
536	537	522	522
503	505	543	541
505	511	532	532
514	515	549	546
490	504	520	519
510	508	525	524
513	498	526	527
521	490	531	532
501	502	531	531
531	540	511	512
541	534	546	545
535	537	571	569
548	546	537	539
544	545	542	542
530	529	532	530
535	537	543	544
528	530	521	523
539	541	565	564
527	525	540	541
529	532	532	535
533	536	525	527
536	539	537	535

545	547	549	550
549	549	533	534
532	534	527	527
524	526	543	542
547	546	528	526
547	548	524	523
539	538	515	515
542	545	532	533
532	535	569	566
528	527	546	544
541	543	554	558
539	537	547	545
511	510	563	565
525	524	528	527
520	524	530	531
528	530	529	529
543	547	531	533
522	521	534	535
505	504	540	542
539	535	550	548
534	536	538	538
526	526	509	511
514	515	519	520
528	527	580	581
537	536	540	542
521	520	526	526
524	528	538	536
535	534	547	546
538	536	517	517
537	532	534	531
540	541	539	541
554	556	527	527
526	530	546	546
532	535	533	538
518	519	598	596
529	526	526	530
533	531	502	508
544	548	533	538
549	550	587	584
546	547	496	486
536	536	510	512
		542	537
		498	512
		546	544
		489	488

Anova: Single Factor

SUMMARY				
Groups	*Sample size*	*Sum*	*Average*	*Variance*
RE(NOND)	82	43121	525.8659	275.5743752
LE(NOND)	82	43184	526.6341	255.1484493
RE(D)	86	45929	534.0581	357.5377565
LE(D)	86	45955	534.3605	339.880301

By looking at average CCT of two different groups, diabetic group has greater value of CCT average

ANOVA

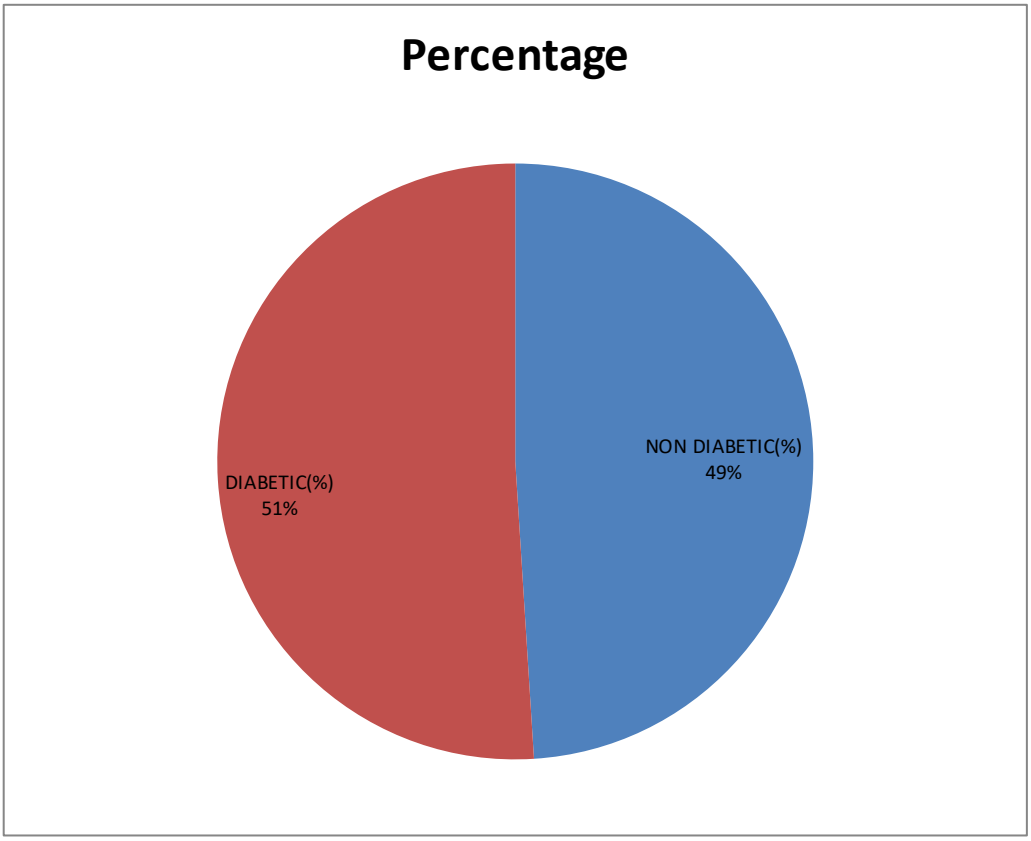
Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups, SSB	5346.556	k-1=3	1782.185	5.785575987	0.000726	2.631811
Within Groups,SSW	102269.1	N-k=332	308.0394			
Total	107615.6	335				

Table 4: Comparison of mean CCT between diabetics and non-diabetics

CALCULATED F VALUE (5.78)>TABULATED F VALUE (2.63), IT IS INFERRED THAT THERE IS SIGNIFICANT DIFFERENCE (INCERASE IN CCT VALUE IN DIABETIC GROUP COMPARED TO NON-DIABETIC GROUP). SINCE P=0.000726 <0.05, NULL HYPOTHESIS IS REJECTED

N=Total No. Of CCT values within groups:

k=No. of columns



Graph 1: Distribution of cases and controls

- **Comparison between LE CCT & RE CCT of diabetic group <= 10yrs AND comparison between LE CCT & RE CCT of diabetic group diabetic group> 10 years**

SAMPLE SIZE OF DIABETIC =<10 years =46

CCT	
RE	LE
524	523
519	522
544	542
529	531
521	523
525	527
539	537
531	531
555	558
526	525
543	541
525	524
511	512
571	569

537	539
542	542
543	544
521	523
540	541
525	527
533	534
527	527
528	526
532	533
547	545
563	565
528	527
530	531
529	529
531	533
534	535
538	538
519	520
538	536
517	517
539	541
527	527
533	538
526	530
502	508
533	538
587	584
496	486
510	512
542	537
489	488

Anova: Single Factor

SUMMARY						
Groups	*Count*	*Sum*	*Average*	*Variance*	*Standard Deviation*	*Max.Value*
RE	46	24449	531.5	294.7889	17.16941726	587
LE	46	24466	531.8696	294.6937	17.16664556	584
ANOVA						
Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	3.141304	1	3.141304	0.010658	0.918004731	3.946876
Within Groups	26526.72	90	294.7413			
Total	26529.86	91				

Table 5: Comparison of mean CCT between right eye and left eye in diabetics less than or equal to 10 years.

CALCULATED F VALUE (0.0106) < TABULATED F VALUE (3.946), IT IS INFERRED THAT THERE IS NO SIGNIFICANT DIFFERENCE IN CCT VALUES OF RE AND LE OF DIABETIC AGE GROUP OF <=10 years

SAMPLE SIZE OF DIABETIC >10 years =40

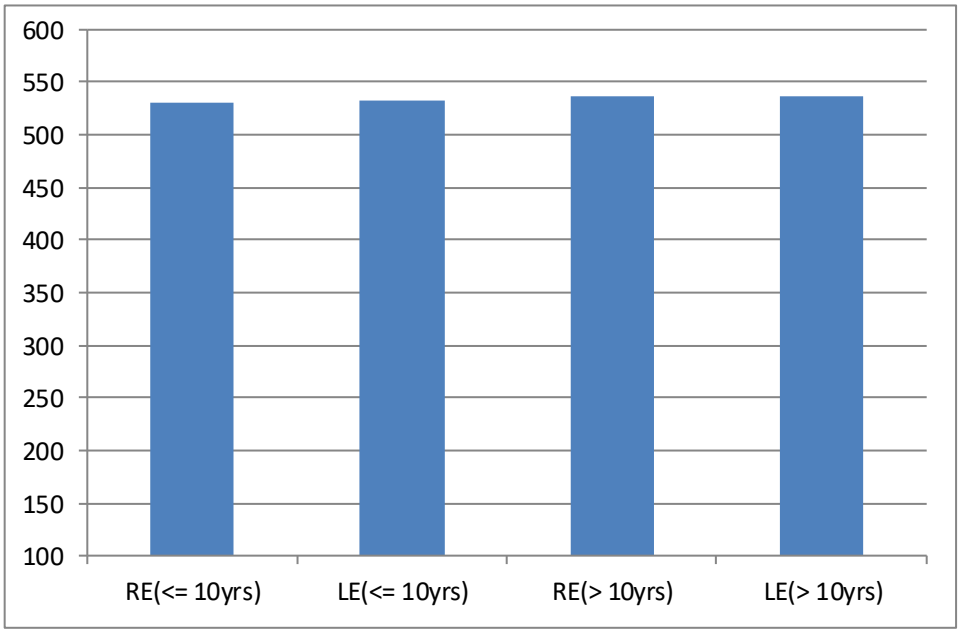
CCT	
RE	LE
501	504
536	530
535	539
520	519
504	508
523	526
526	521
530	530
568	571
522	522
532	532
549	546
520	519
526	527
531	532
531	531
546	545
532	530
565	564
532	535
537	535
549	550
543	542
524	523
515	515
569	566
546	544
554	558
540	542
550	548
509	511
580	581
540	542
526	526
547	546
534	531
546	546
598	596
498	512
546	544

Anova: Single Factor

SUMMARY						
Groups	*Count*	*Sum*	*Average*	*Variance*	*Standard Deviation*	*Max.Value*
RE	40	21480	537	422.5128	20.55511665	598
LE	40	21489	537.225	384.9994	19.62140054	596
ANOVA						
Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	1.0125	1	1.0125	0.002508	0.960189073	3.963472
Within Groups	31492.98	78	403.7561			
Total	31493.99	79				

Table 6: Comparison of mean CCT between right eye and left eye in diabetics more than 10 years

CALCULATED F VALUE (0.0025) < TABULATED F VALUE (3.963), IT IS INFERRED THAT THERE IS NO SIGNIFICANT DIFFERENCE IN CCT VALUES OF RE AND LE OF DIABETIC AGE GROUP OF >10 years. SINCE P=0.960 >0.05, NULL HYPOTHESIS IS ACCEPTED



Graph 2: CCT averages in diabetics ≤10 years duration and >10yrs duration

- **Comparison of CCT between diabetic groups of ≤10 years duration AND >10 years duration**

SAMPLE SIZE OF DIABETIC =<10 years =46

SAMPLE SIZE OF DIABETIC >10 years =40

CCT (=<10 yrs.)		CCT (>10 yrs.)	
RE (=<10 yrs.)	LE(=10 yrs.)	RE(>10 yrs)	LE(>10 yrs)
524	523	501	504
519	522	536	530
544	542	535	539
529	531	520	519
521	523	504	508
525	527	523	526
539	537	526	521
531	531	530	530
555	558	568	571
526	525	522	522
543	541	532	532
525	524	549	546
511	512	520	519
571	569	526	527
537	539	531	532
542	542	531	531
543	544	546	545
521	523	532	530
540	541	565	564
525	527	532	535
533	534	537	535
527	527	549	550
528	526	543	542
532	533	524	523
547	545	515	515
563	565	569	566
528	527	546	544
530	531	554	558
529	529	540	542
531	533	550	548
534	535	509	511
538	538	580	581
519	520	540	542
538	536	526	526
517	517	547	546
539	541	534	531
527	527	546	546
533	538	598	596
526	530	498	512
502	508	546	544
533	538		
587	584		
496	486		
510	512		
542	537		
489	488		

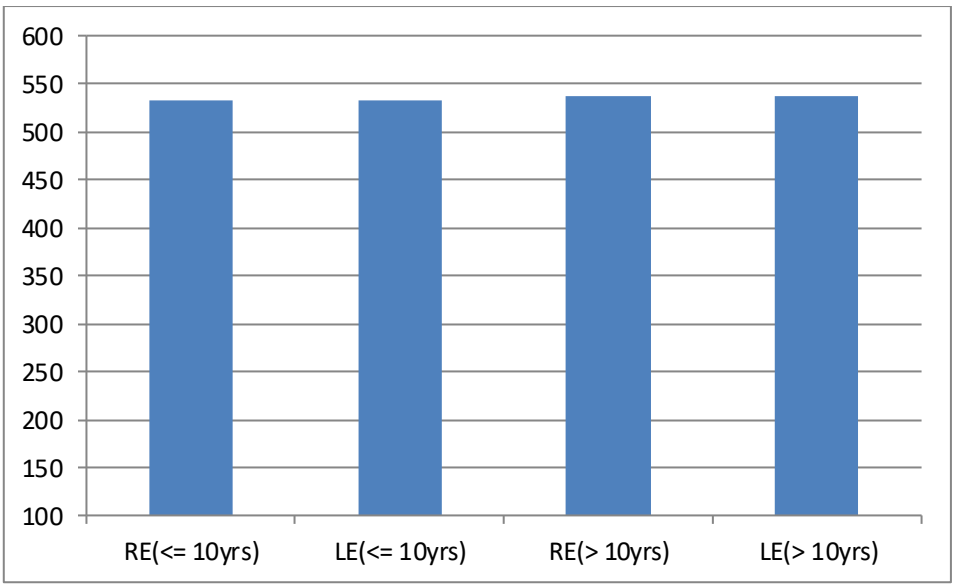
Anova: Single Factor

SUMMARY				
Groups	*Count*	*Sum*	*Average*	*Variance*
RE(=<10 yrs)	46	24449	531.5	294.7889
LE(=<10 yrs)	46	24466	531.8696	294.6937
RE(>10 yrs)	40	21480	537	422.5128
LE(>10 yrs)	40	21489	537.225	384.9994

ANOVA						
Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	1264.773	3	421.5909	1.220745	0.30384	2.658399
Within Groups	58019.69	168	345.3553			
Total	59284.47	171				

Table 7: Comparison of mean CCT between diabetics more than 10 years duration and less than or equal to 10 years duration.

CALCULATED F VALUE(1.220)<TABULATED F VALUE(2.658),IT IS INFERRED THAT THERE IS NO SIGNIFICANT DIFFERENCE OF CCT AVERAGES OF THESE TWO GROUPS, HOWEVER BY COMPARING AVERAGES,DIABETIC >10yrs GROUP HAS RELATIVELY HIGHER AVERAGES OF CCT. SINCE P=0.303 >0.05, NULL HYPOTHESIS IS ACCEPTED



CCT AVERAGES FOR ≤10 years AND >10years

- **Association between NPDR AND CCT**

SAMPLE SIZE NPDR -25

CCT		CCT	
RE	**LE**	**RE(NPDR)**	**LE(NPDR)**
524	523	524	523
501	504	521	523
519	522	523	526
544	542	539	537
536	530	555	558
529	531	549	546
521	523	525	524
535	539	531	531
520	519	546	545
525	527	537	539
504	508	532	535
523	526	537	535
539	537	527	527
526	521	543	542
530	530	515	515
531	531	546	544
568	571	540	542
555	558	550	548
526	525	509	511
522	522	540	542
543	541	526	526
532	532	538	536
549	546	517	517
520	519	546	546
525	524	546	544
526	527		
531	532		
531	531		
511	512		
546	545		
571	569		
537	539		
542	542		
532	530		
543	544		
521	523		
565	564		
540	541		
532	535		
525	527		
537	535		
549	550		

533	534		
527	527		
543	542		
528	526		
524	523		
515	515		
532	533		
569	566		
546	544		
554	558		
547	545		
563	565		
528	527		
530	531		
529	529		
531	533		
534	535		
540	542		
550	548		
538	538		
509	511		
519	520		
580	581		
540	542		
526	526		
538	536		
547	546		
517	517		
534	531		
539	541		
527	527		
546	546		
533	538		
598	596		
526	530		
502	508		
533	538		
587	584		
496	486		
510	512		
542	537		
498	512		
546	544		
489	488		

CCT(SEVERE)	
RE(NPDR SEVERE)	LE(NPDR SEVERE)
521	523
546	545
546	544
537.67	537.33

CCT(MODERATE)	
RE(NPDR MODERATE)	LE(NPDR MODERATE)
523	526
539	537
555	558
549	546
525	524
532	535
543	542
515	515
540	542
550	548
540	542
526	526
538	536
546	546
537.2143	537.3571

CCT(MILD)	
RE(NPDR MILD)	LE(NPDR MILD)
524	523
531	531
537	539
537	535
527	527
509	511
517	517
546	544
528.5	528.38

PDR(CCT)	
RE(PDR)	**LE(PDR)**
568	571
571	569
565	564
549	550
532	533
569	566
554	558
563	565
580	581
587	584
563.8	564.1

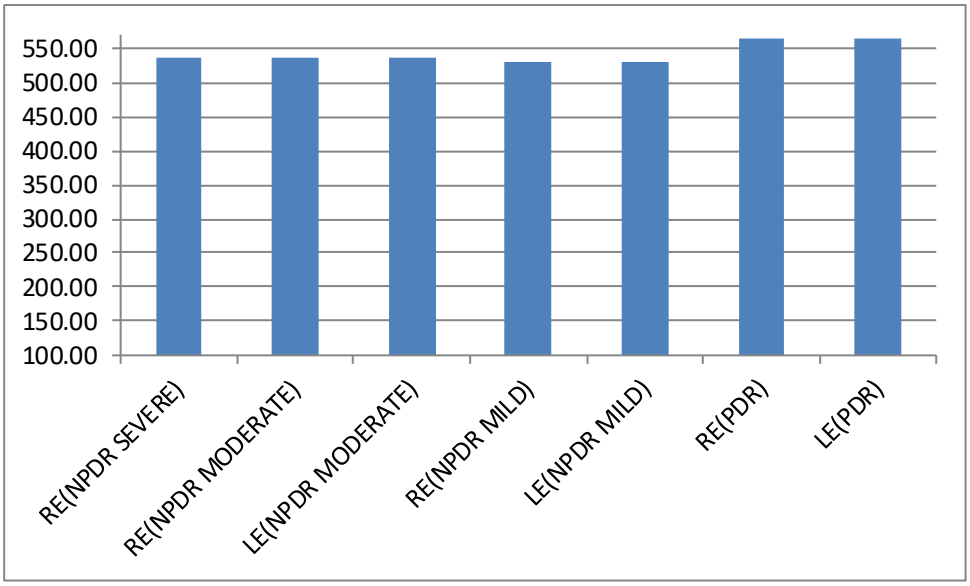
Anova: Single Factor

SUMMARY						
Groups	*Count*	*Sum*	*Average*	*Variance*		
RE	86	45929	534.0581	357.537756		
LE	86	45955	534.3605	339.880301		
RE(NPDR)	25	13362	534.48	149.01		
LE(NPDR)	25	13362	534.48	138.093333		
ANOVA						
Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	6.7689	3	2.2563	0.00743337	0.999117	2.646014
Within Groups	66171.01	218	303.5368			
Total	66177.78	221				

Table 8: Comparison of mean CCT among diabetics with mild, moderate and severe NPDR

CALCULATED VALUE OF F (0.007433) <TABULATED VALUE OF F (2.646), IT IS INFERRED THAT THERE IS NO SIGNIFICANT DIFFERENCE IN CCT VALUES AMONG MILD, MODERATE& SEVERE NPDR GROUPS. SINCE P=0.999 >0.05, NULL HYPOTHESIS IS ACCEPTED

Proportion of NPDR patients over diabetic population	25/86	0.290698
Proportion of PDR patients over diabetic population	10/86	0.116279



Graph 3: Mean CCT of mild, moderate and severe NPDR AND PDR

- **Association between PDR AND CCT**

TOTAL NUMBER OF PATIENTS WITH PDR =10

CCT		CCT	
RE	**LE**	**RE(PDR)**	**LE(PDR)**
524	523	568	571
501	504	571	569
519	522	565	564
544	542	549	550
536	530	532	533
529	531	569	566
521	523	554	558
535	539	563	565
520	519	580	581
525	527	587	584
504	508		
523	526		
539	537		
526	521		
530	530		
531	531		
568	571		
555	558		
526	525		
522	522		
543	541		
532	532		
549	546		
520	519		
525	524		
526	527		
531	532		
531	531		
511	512		
546	545		
571	569		
537	539		
542	542		
532	530		
543	544		
521	523		
565	564		
540	541		
532	535		
525	527		
537	535		
549	550		
533	534		
527	527		
543	542		
528	526		

524	523		
515	515		
532	533		
569	566		
546	544		
554	558		
547	545		
563	565		
528	527		
530	531		
529	529		
531	533		
534	535		
540	542		
550	548		
538	538		
509	511		
519	520		
580	581		
540	542		
526	526		
538	536		
547	546		
517	517		
534	531		
539	541		
527	527		
546	546		
533	538		
598	596		
526	530		
502	508		
533	538		
587	584		
496	486		
510	512		
542	537		
498	512		
546	544		
489	488		

Anova: Single Factor

SUMMARY						
Groups	*Count*	*Sum*	*Average*	*Variance*		
RE	86	45929	534.0581	357.5378		
LE	86	45955	534.3605	339.8803		
RE(PDR)	10	5638	563.8	247.2889		
LE(PDR)	10	5641	564.1	217.8778		
ANOVA						
Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	15851.83	3	5283.945	15.65193	3.96E-09	2.652646
Within Groups	63467.03	188	337.5906			
Total	79318.87	191				

Table 9: Comparison of mean CCT between diabetics with PDR and diabetics without PDR

CALCULATED VALUE OF F (15.651)>>TABULATED VALUE OF F (2.652), IT IS INFERRED THAT THERE IS SIGNIFICANT DIFFERENCE IN CCT VALUES OF PDR GROUP IN COMPARISION WITH THE POPULATION SINCE P=0.0000000039 <0.05, NULL HYPOTHESIS IS REJECTED

- **Association between GENDER AND CCT**

CCT		CCT	
RE(M)	**LE(M)**	**RE(FM)**	**LE(FM)**
536	530	533	536
549	550	525	524
565	564	526	526
539	541	537	532
544	545	537	535
540	541	568	571
528	530	598	596
546	546	510	522
554	558	510	508
580	581	517	517
548	546	519	520
502	510	537	539
526	525	533	531
532	535	505	504
534	536	507	505
525	527	524	528

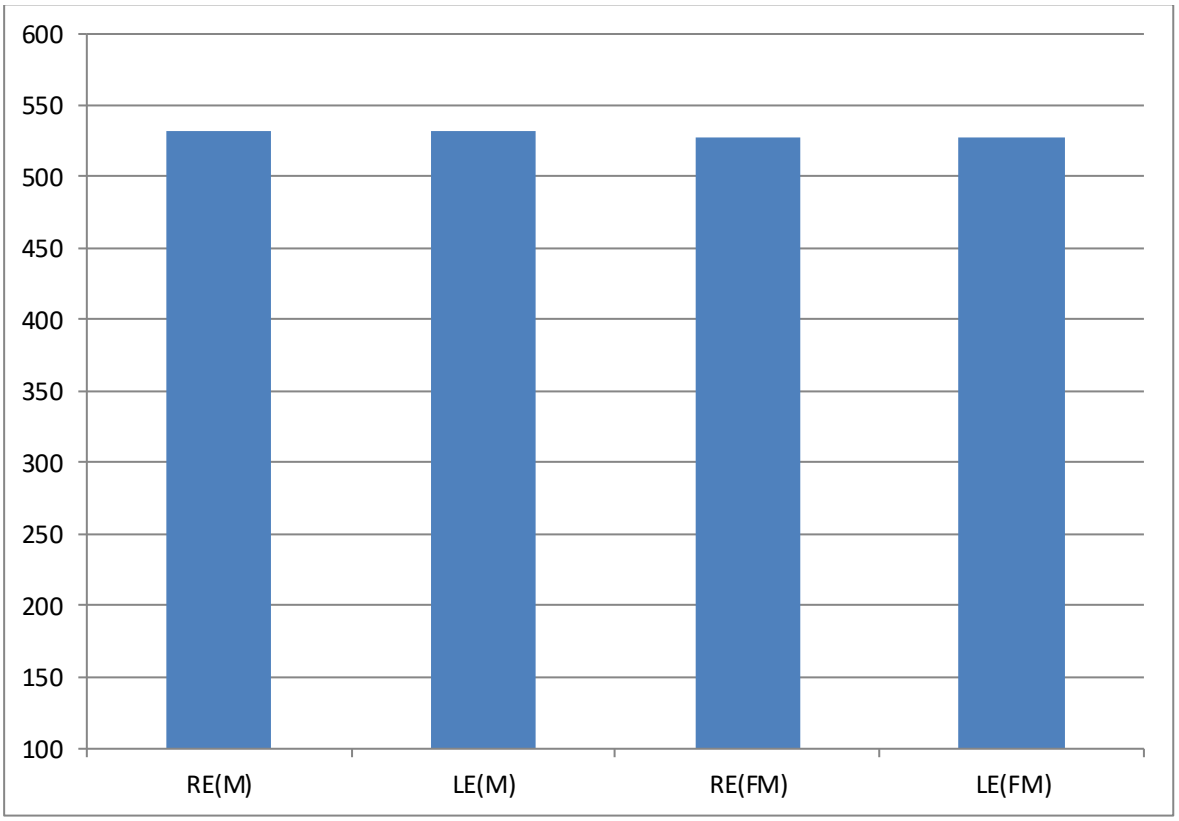
534	535	529	529
514	515	531	531
513	498	537	536
489	488	546	544
515	515	543	541
533	538	498	512
542	537	533	534
547	546	478	480
532	530	503	505
532	533	504	508
527	525	505	511
541	534	522	521
542	542	524	523
543	544	525	527
533	531	528	530
531	531	529	532
540	542	530	529
540	542	531	532
546	547	532	530
547	546	534	531
549	550	539	541
587	584	539	537
484	501	540	541
535	539	542	545
521	520	543	542
532	532	544	548
549	546	555	558
527	527	510	512
528	525	514	515
536	537	550	548
539	537	514	518
543	547	531	540
520	519	549	549
547	545	496	486
502	508	519	522
503	502	521	523
520	524	522	522
520	519	526	530
524	526	529	526
531	532	530	531
535	537	532	535
536	539	536	536
538	536	538	538
540	542	538	536
545	547	539	535
546	545	528	527
547	548	531	533
554	556	529	531
569	566	521	490
526	521	544	542
526	530	490	504
509	511	494	501
532	535	523	526

563	565	528	526
571	569	532	534
501	504	541	543
511	512	483	499
512	514		
524	518		
525	524		
526	527		
526	526		
528	527		
535	534		
511	510		
521	523		
546	544		
502	503		
530	530		
501	502		
524	523		
539	538		
525	522		
528	527		
511	509		
527	527		
535	537		
518	519		
533	538		

Anova: Single Factor						
SUMMARY						
Groups	*Count*	*Sum*	*Average*	*Variance*		
RE(M)	95	50562	532.2316	316.8607		
LE(M)	95	50589	532.5158	301.3588		
RE(FM)	73	38488	527.2329	343.2367		
LE(FM)	73	38550	528.0822	318.382		
ANOVA						
Source of Variation	*SS*	*Df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	1866.46	3	622.1535	1.953253	0.120841	2.631811
Within Groups	105749.2	332	318.5216			
Total	107615.6	335				

Table 10: Comparison of mean CCT between males and females

CALCULATED VALUE OF F (1.95) <TABULATEDVALUE OF F (2.63), IT IS INFERRED THAT THERE NO SIGNIFICANT DIFFERENCE IN CCT VALUES OF MALE GROUP IN COMPARISION WITH THE FEMALE GROUP.HOWEVER BASED ON THE ABOVE GRAPH MALE GROUP HAS SLIGHTLY LARGER VALUE OF CCT AVERAGE COMPARED TO THAT OF FEMALE GROUP. SINCE P=0.12 >0.05, NULL HYPOTHESIS IS ACCEPTED



Graph 4: GENDER Vs CCT

- **COMPARISION OF CCT BETWEEN MALE DIABETICS AND FEMALE DIABETICS**

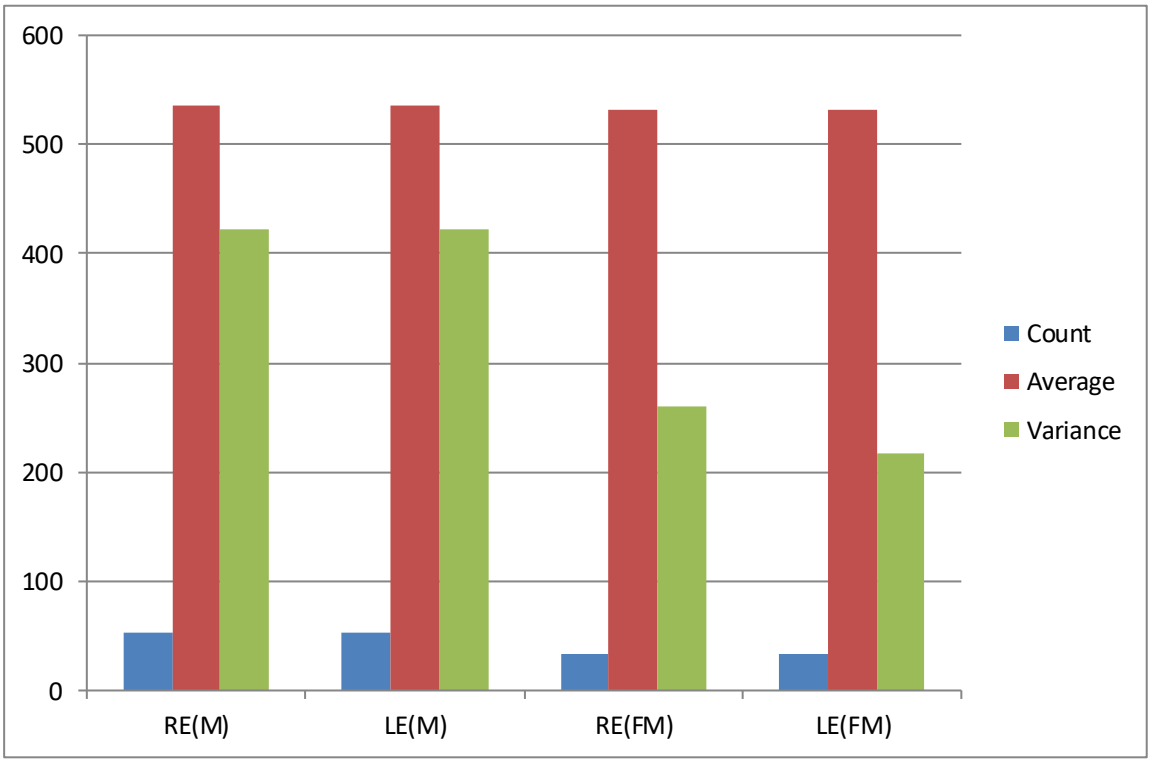
CCT		CCT	
RE(M)	LE(M)	RE(FM)	LE(FM)
501	504	524	523
519	522	544	542
536	530	529	531
521	523	520	519
535	539	531	531
525	527	555	558
504	508	526	525
523	526	522	522
539	537	543	541
526	521	549	546
530	530	520	519
568	571	525	524
532	532	531	531
526	527	511	512
531	532	537	539
546	545	565	564
571	569	532	535
542	542	549	550
532	530	527	527
543	544	528	526
521	523	524	523
540	541	532	533
525	527	569	566
537	535	534	535
533	534	509	511
543	542	540	542
515	515	547	546
546	544	546	546
554	558	533	538
547	545	502	508
563	565	533	538
528	527	510	512
530	531	542	537
529	529	498	512
531	533		
540	542		
550	548		
538	538		
519	520		
580	581		
526	526		

538	536		
517	517		
534	531		
539	541		
527	527		
598	596		
526	530		
587	584		
496	486		
546	544		
489	488		

Anova: Single Factor							
SUMMARY							
Groups	*Count*	*Sum*	*Average*	*Variance*			
RE(M)	52	27842	535.4231	422.2881			
LE(M)	52	27843	535.4423	422.4476			
RE(FM)	34	18087	531.9706	260.8779			
LE(FM)	34	18112	532.7059	217.9109			
ANOVA							
Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*	
Between Groups	402.9165	3	134.3055	0.383199	0.765241	2.658399	
Within Groups	58881.55	168	350.4854				
Total	59284.47	171					

Table 11: Comparison of mean CCT between male and female diabetics.

CALCULATED VALUE OF F (0.38) <=TABULATED VALUE OF F (2.66), IT IS INFERRED THAT THERE NO SIGNIFICANT DIFFERENCE IN CCT VALUES OF DIABETIC MALE GROUP IN COMPARISION WITH THE DIABETIC FEMALE GROUP.HOWEVER BASED ON THE GRAPH MALE GROUP HAS LARGER VARIANCE OF CCT COMPARED TO THAT OF FEMALE GROUP.THERE IS NO SIGNIFICANT DIFFERENCE IN AVERAGES CCT's OF DIABETIC MALE AND FEMALE GROUP. SINCE P=0.76 >0.05, NULL HYPOTHESIS IS ACCEPTED



Graph 5: GENDER Vs CCT (DIABETICS)

- **ASSOCIATION B/W AGE AND CCT**

	CCT	
AGE	**RE**	**LE**
60	502	510
75	483	499
61	524	518
54	532	530
70	514	518
70	478	480
65	507	505
58	525	522
75	540	542
70	512	514
48	503	502
74	494	501
65	528	525
65	511	509
60	484	501
60	533	531
60	510	522
53	531	532
55	502	503
68	536	537
50	503	505
50	505	511
61	533	538
79	598	596
72	514	515
70	490	504
70	510	508
53	526	530
62	502	508
61	533	538
52	587	584
55	496	486
50	510	512
80	513	498
65	542	537
50	498	512
65	521	490
65	501	502
64	546	544
69	531	540
62	489	488
65	541	534
72	535	537
60	548	546
65	544	545
70	530	529
70	535	537
65	528	530

55	539	541
60	527	525
75	529	532
78	533	536
70	536	539
50	545	547
40	549	549
60	532	534
65	524	526
40	547	546
67	547	548
66	539	538
48	542	545
70	532	535
70	528	527
57	541	543
63	539	537
79	511	510
63	525	524
60	520	524
78	528	530
45	543	547
70	522	521
70	505	504
67	539	535
60	534	536
65	526	526
68	514	515
55	528	527
60	537	536
74	521	520
65	524	528
60	535	534
62	538	536
55	537	532
65	540	541
60	554	556
67	526	530
60	532	535
70	518	519
65	529	526
68	533	531
62	544	548
56	549	550
48	546	547
56	536	536
52	524	523
84	501	504
55	519	522
37	544	542
58	536	530
59	529	531
49	521	523

50	535	539
60	520	519
65	525	527
79	504	508
70	523	526
61	539	537
63	526	521
65	530	530
65	531	531
38	568	571
55	555	558
43	526	525
50	522	522
43	543	541
65	532	532
65	549	546
65	520	519
60	525	524
77	526	527
63	531	532
65	531	531
60	511	512
42	546	545
60	571	569
60	537	539
44	542	542
60	532	530
65	543	544
57	521	523
70	565	564
55	540	541
60	532	535
57	525	527
63	537	535
57	549	550
57	533	534
60	527	527
43	543	542
60	528	526
69	524	523
65	515	515
55	532	533
60	569	566
65	546	544
72	554	558
45	547	545
60	563	565
65	528	527
64	530	531
55	529	529
46	531	533
62	534	535
60	540	542

62	550	548
38	538	538
61	509	511
65	519	520
45	580	581
60	540	542
69	526	526
38	538	536
49	547	546
65	517	517
69	534	531
45	539	541
60	527	527
49	546	546

	AGE	*RE*
AGE	1	
RE	-0.26541	1

Table 12: a) Correlation between age and CCT

Negative correlation is a relationship between two variables in which one variable increases another decreases and vice versa. In statistics, a perfect negative correlation is represented by value -1, a zero indicates no correlation and a +1 indicates a perfect positive correlation. Correlation coefficient arrived through data analysis tool in MS excel. Here it is -0.2654 is an indication that these two variables are having poor inverse correlation

	LE	*AGE*
LE	1	
AGE	-0.27094	1

Table 12: b) Correlation between age and CCT

Negative correlation is a relationship between two variables in which one variable increases another decreases and vice versa. In statistics, a perfect negative correlation is represented by value -1, a zero indicates no correlation and a +1 indicates a perfect positive correlation. Correlation coefficient arrived through data analysis tool in MS excel. Here it is -0.27094 is an indication that these two variables are having poor inverse correlation

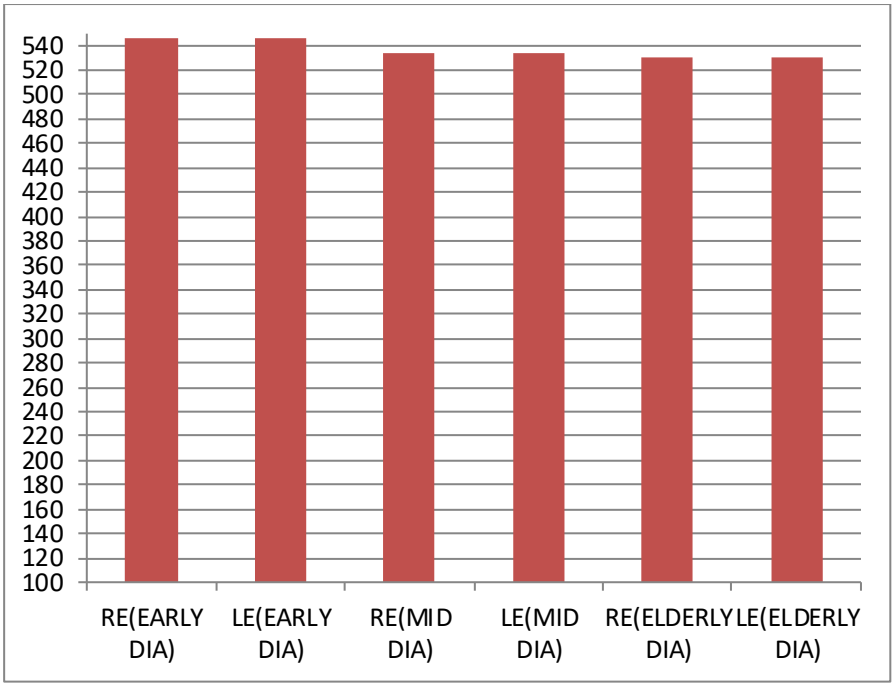
- **Association between elderly diabetics and CCT**

<=45		>46 TO <=60		>60 TO ABOVE	
CCT		CCT		CCT	
RE(EARLY DIA)	LE(EARLY DIA)	RE(MID DIA)	LE(MID DIA)	RE(ELDERLY DIA)	LE(ELDERLY DIA)
544	542	524	523	501	504
568	571	519	522	525	527
526	525	536	530	504	508
543	541	529	531	523	526
546	545	521	523	539	537
542	542	535	539	526	521
543	542	520	519	530	530
547	545	555	558	531	531
538	538	522	522	532	532
580	581	525	524	549	546
538	536	511	512	520	519
539	541	571	569	526	527
		537	539	531	532
		532	530	531	531
		521	523	543	544
		540	541	565	564
		532	535	537	535
		525	527	524	523
		549	550	515	515
		533	534	546	544
		527	527	554	558
		528	526	528	527
		532	533	530	531
		569	566	534	535
		563	565	550	548
		529	529	509	511
		531	533	519	520
		540	542	526	526
		540	542	517	517
		547	546	534	531
		527	527	533	538
		546	546	598	596
		526	530	502	508
		587	584	533	538
		496	486	542	537
		510	512	546	544
		498	512	489	488

Anova: Single Factor						
SUMMARY						
Groups	*Count*	*Sum*	*Average*	*Variance*		
RE(EARLY DIA)	12	6554	546.1667	205.0606		
LE(EARLY DIA)	12	6549	545.75	232.2045		
RE(MID DIA)	37	19733	533.3243	350.2252		
LE(MID DIA)	37	19757	533.973	335.6937		
RE(ELDERLY DIA)	37	19642	530.8649	371.3979		
LE(ELDERLY DIA)	37	19649	531.0541	341.2192		
ANOVA						
Source of Variation	*SS*	*Df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	4127.251	6	687.8752	2.057744	0.060879	2.153911
Within Groups	55157.21	165	334.2861			
Total	59284.47	171				

Table 13: Comparison of mean CCT among diabetics less than or equal to 45 years, 46 to 60 years and >60 years

CALCULATED VALUE OF F (2.057) SLIGHTLY LESSER THAN TABULATED VALUE OF F (2.153), IT IS INFERRED THAT THERE IS NO SIGNIFICANT DIFFERENCE IN CCT VALUES OF DIFFERENT AGE GROUPS AND BY LOOKING AT THE AVERAGE CCT's, ELDERLY DIABETIC GROUP HAS LESSER CCT AVERAGE COMPARED TO EARLY DIABETIC GROUPS. SINCE P=0.060 >0.05, NULL HYPOTHESIS IS ACCEPTED



Graph 6: Mean CCT of DIFFERENT AGE GROUPS OF diabetic patients

- **Association between diabetic CCT(RE) and RBS**

RE	RBS
524	199
501	187
519	171
544	78
536	198
529	102
521	156
535	178
520	143
525	123
504	154
523	99
539	100
526	177
530	152
531	158
568	128
555	180
526	132
522	167
543	91
532	139
549	90
520	129

525	89
526	193
531	89
531	75
511	86
546	88
571	190
537	92
542	126
532	145
543	96
521	131
565	199
540	94
532	198
525	125
537	160
549	79
533	169
527	111
543	109
528	104
524	75
515	100
532	96
569	101
546	129
554	129
547	76
563	198
528	90
530	170
529	123
531	134
534	125
540	198
550	189
538	100
509	139
519	157
580	199
540	119
526	111
538	80
547	107
517	156

534	180
539	123
527	125
546	114
533	124
598	118
526	156
502	180
533	122
587	199
496	81
510	198
542	131
498	178
546	163
489	121

	RE	*RBS*
RE	1	
RBS	0.046404194	1

Positive correlation is a relationship between two variables in which one variable increases as other increases. In statistics, a perfect positive correlation is represented by value +1, a zero indicates no correlation and a -1 indicates a perfect negative correlation. Correlation co-efficient arrived through data analysis tool in MS excel. Here it is 0.046404 is an indication that these two variables are having poor proportion correlation

- **Association between diabetic CCT(RE) and FBS**

519	89
544	99
536	111
529	101
521	116
535	81
520	99
525	107
504	125
523	100
539	119
526	109

530	79
531	97
568	121
555	120
526	103
522	89
543	90
532	78
549	115
520	117
525	109
526	103
531	111
531	77
511	95
546	125
571	121
537	120
542	122
532	117
543	92
521	102
565	97
540	99
532	111
525	112
537	111
549	116
533	92
527	95
543	98
528	79
524	78
515	114
532	96
569	117
546	119
554	102
547	120
563	61
528	115
530	98
529	93
531	79
534	104
540	86
550	121

538	121
509	102
519	120
580	108
540	102
526	101
538	124
547	105
517	116
534	99
539	109
527	98
546	105
533	102
598	118
526	124
502	121
533	100
587	125
496	81
510	125
542	79
498	101
546	102
489	77

	RE	*FBS*
RE	1	
FBS	0.163762	1

Positive correlation is a relationship between two variables in which one variable increases as other increases. In statistics, a perfect positive correlation is represented by value +1, a zero indicates no correlation and a -1 indicates a perfect negative correlation. Correlation coefficient arrived through data analysis tool in MS excel. Here it is 0.163762 is an indication that these two variables are having considerable proportion correlation. Covariance tells us that in which direction change will take place but not magnitude of relationship,

The advantage of correlation is that magnitude of relationship can be known. Here positive correlation of 0.163 indicates 1.63% increase in FBS will result in 10% increase in CCT (RE)

- **Association between diabetic CCT(RE) and PPBS**

RE	PPBS
524	177
501	187
519	142
544	156
536	123
529	189
521	199
535	178
520	120
525	119
504	157
523	192
539	166
526	151
530	176
531	152
568	134
555	154
526	198
522	161
543	195
532	195
549	172
520	170
525	180
526	131
531	128
531	176
511	196
546	178
571	145
537	162
542	178
532	154
543	100
521	128
565	167
540	148
532	92
525	123
537	180
549	149
533	150

527	177
543	145
528	167
524	139
515	160
532	148
569	159
546	181
554	199
547	194
563	150
528	168
530	180
529	167
531	147
534	136
540	197
550	182
538	174
509	176
519	199
580	167
540	198
526	170
538	159
547	154
517	41
534	132
539	178
527	198
546	156
533	146
598	183
526	199
502	184
533	199
587	189
496	168
510	187
542	173
498	198
546	189
489	132

	RE	*PPBS*
RE	1	

PPBS	0.037918	1

Positive correlation is a relationship between two variables in which one variable increases as other increases. In statistics, a perfect positive correlation is represented by value +1, a zero indicates no correlation and a -1 indicates a perfect negative correlation. Correlation coefficient arrived through data analysis tool in MS excel. Here it is 0.037918 is an indication that these two variables are having poor proportion correlation

- **Association between CCT(RE) diabetic and HbA1C**

RE	HbA1C
524	6.2
501	7
519	6.9
544	6.8
536	6.2
529	6.8
521	7
535	6.7
520	5.8
525	5.7
504	7.1
523	6.1
539	5.9
526	7.2
530	7
531	7
568	7.2
555	5.4
526	7.1
522	5.1
543	7
532	6.6
549	6
520	5.8
525	7.2
526	6.5
531	6.1
531	7.2

511	7.1
546	7
571	7.2
537	7
542	7.2
532	5.5
543	5.9
521	6.4
565	5
540	5.9
532	7
525	7.2
537	6.4
549	6
533	6.7
527	7.2
543	5
528	5.8
524	6.3
515	5.4
532	6
569	6.6
546	6.7
554	7.2
547	7.1
563	6.8
528	6.4
530	5.6
529	7
531	7.2
534	6
540	6.2
550	5.7
538	6.5
509	5.9
519	6
580	7.1
540	5.9
526	6.1
538	6.4
547	5.8
517	5.8
534	4.9
539	5.9
527	5
546	5.6
533	6.2

598	7
526	6.9
502	7.2
533	7
587	7.2
496	6.5
510	7
542	6.6
498	7
546	6.1
489	6

	RE	*HbA1C*
RE	1	
HbA1C	0.046277	1

Positive correlation is a relationship between two variables in which one variable increases as other increases. In statistics, a perfect positive correlation is represented by value +1, a zero indicates no correlation and a -1 indicates a perfect negative correlation. Correlation coefficient arrived through data analysis tool in MS excel. Here it is 0.046277 is an indication that these two variables are having poor proportion correlation

DISCUSSION

Diabetes mellitus affects all structures of the eye. Other than diabetic retinopathy patients can also develop corneal damage such as endothelial defects, punctate epithelial keratopathy, recurrent corneal erosions and persistent epithelial defects. In diabetic individuals there is polymegathism, pleomorphism and reduction in density of corneal endothelial cells as compared to non-diabetic individuals. Recent studies have shown advanced glycosylated end product act as cross-linking agents to increase the covalent bond in corneal stroma and eventually its thickness. The central corneal thickness in diabetics signifies functional and morphological status of cornea. This may interfere with susceptibility to surgical stress and delayed healing after intraocular surgery like cataract surgery, refractive surgery. [72]

In our present study, the mean CCT in diabetics was 534.0581µ in right eye and 534.3605µ in left eye and in non-diabetics it was 525.8659µ in right eye and 526.6341µ in the left eye. Since the calculated F value (5.78) > tabulated F value (2.63), it is inferred that there is significant difference (increase in CCT value in diabetic group compared to non-diabetic group; $P = 0.000726 < 0.05$ by ANOVA test). This is in accordance with the studies reported by Busted N et al who found that diabetic corneas were significantly thicker than the normal corneas in a sample size of 81 diabetic subjects. [48] Ozdamar Y et al in 2010 also reported that the CCTs of diabetic patients were thicker than that of normal subjects. [65] Storr-Paulsen et al. studied 107 patients with type II DM and 128 nondiabetic controls and concluded that CCT was increased among type II diabetes patients compared to controls. [2]

In our study, there is no significant difference in mean CCT values between right eye and left eye among diabetics less than or equal to 10 years duration (calculated F value 0.0106<tabulated F value 3.946; P value 0.918004 >0.05). Also, there is no significant difference in mean CCT between right eye and left eye among diabetics more than 10 years duration (calculated F value 0.0025 <tabulated F value 3.963; P value 0.960 >0.05).

The effect of duration of diabetes on corneal thickness was studied by Lee et al who reported that central corneal thickness was significantly higher for diabetes of over 10 years' duration than for diabetes of under 10 years' duration. [47] In our study also the mean CCT in subjects with diabetes of more than10 years duration was higher(537µ) than those having it for less than or equal to10 years(531µ), but the difference was not statistically significant. (calculated F value 1.220 < tabulated F value 2.658; P=0.303> 0.05).

In the current study, no significant difference was found in CCT between the three diabetic subgroups i.e., those with mild NPDR, those with moderate NPDR and those with severe NPDR (calculated F value 0.007433 < tabulated F value 2.646; P=0.999 >0.05). Busted et al. [48] and Wiemer et al. [27] also found that CCT increased in DM regardless of the severity of the retinal disease.

In our study, we found a statistically significant difference in CCT between diabetics with PDR and diabetics without PDR (CCT was much thicker among diabetics with proliferative diabetic retinopathy; calculated F value 15.651 >> tabulated F value 2.652; P=0.0000000039 <0.05). Ozdamar et al. reported in their

study that patients with proliferative diabetic retinopathy had thicker CCT than those with non-proliferative diabetic retinopathy and no retinopathy; however, the difference was not statistically significant. (65)

We found in this study (both diabetics and non-diabetics), that the mean CCT of males (532.2µ) is greater than mean CCT in females (527.2µ), but the difference is not a statistically significant (calculated F value 1.95 < tabulated F value 2.63; P=0.12 >0.05).

The mean CCT for male subjects in diabetic group in present study (535.4µ) was higher when compared to the female subjects in diabetic group (531.9µ). However, the difference was not statistically significant between the two groups (calculated F value 0.38 < tabulated F value 2.66; P =0.76>0.05). Another study done for Indian eyes have reported significantly higher CCT in males (515.6± 33.8µ) than females (508.0 ± 32.8µ) with p value 0.001. (63)

We observed a decrease in CCT with age in both diabetic and non-diabetic groups. However, the correlation was a poor inverse correlation
(-0.2654 for right eye and -0.27094 for left eye).

In this study, we did not observe any significant difference in mean CCT values among diabetics of different age groups (diabetics ≤45 years of age, diabetics > 46 years and ≤60 years, diabetics > 60 years), as the calculated F value 2.057 < tabulated F value 2.153; P =0.060> 0.05.

We, in our study observed a poor positive correlation between RBS, PPBS, HbA_1C and CCT in type 2 diabetics. This is probably due to the inclusion of study subjects in our study whose glycemic status is relatively under control. Storr Paulsen et al [2], in their study, reported that HbA1c did not have any impact on the CCT. McNamara et al [69] observed positive correlation between HbA1c level and CCT in Type 1 diabetics but reported thicker corneas in diabetics but found no direct correlation with HbA1c level in type 2 diabetes similar to our study. This observation was reinforced by Yasgan S et al [57]

Another study, Mehmet et al [67] reported that diabetic patients with HbA1c levels > 7% had thicker corneas than patients with HbA1c levels < 7% (P = 0.021).

Increase in FBS showed an increase in central corneal thickness. We found a positive correlation between FBS and CCT in type 2 diabetes patients in our study. A position correlation of 0.163 was obtained, which means that 1.63% increase in FBS will result in 10% increase in CCT.

CONCLUSION

- Diabetics showed a higher CCT as compared to non-diabetics.
- Diabetics with PDR showed a higher CCT as compared to diabetics without PDR.
- Age of diabetics irrespective of duration of diabetes did not have significant effect on CCT. Elderly diabetics showed a relatively lesser CCT.
- There is no statistically significant difference in CCT between diabetics of ≤10 years duration and diabetics >10 years duration, but diabetics >10 years have a relatively higher CCT.
- CCT is not affected by the severity of NPDR.
- There is no statistically significant difference in CCT between males and females in diabetics and non-diabetics.
- Increase in CCT was observed with increased FBS values.
- **Henceforth, it is important to measure the central corneal thickness in all diabetics, as it affects the IOP measurement which is vital for early diagnosis and timely treatment of glaucoma.**

SUMMARY

A cross sectional, time bound study was done on type 2 diabetics and nondiabetics, aged above 30 years, attending outpatient and inpatient departments of the hospital to determine association between Central Corneal thickness and type 2 diabetes.

A total of 168 patients, fulfilling the inclusion criteria were included in the study. Their parameters including: central corneal thickness, RBS, FBS, PPBS, HbA1c, intraocular pressure (by applanation tonometry) and fundus changes were noted and studied in detail.

In the present study, mean central corneal thickness is 534.05μm and 534.36μm in right eye and left eye respectively in diabetics. And mean central corneal thickness in nondiabetics is 525.86μm and 526.63μm right eye and left eye respectively. Of the total 168 patients, 51% are diabetics and 49% are non-diabetics.

There is a statistically significant difference in CCT between diabetics and non-diabetics, with a higher CCT in diabetics compared to non-diabetics. No difference in CCT is found between right eye and left eye in both the groups (diabetics and non-diabetics). No difference in CCT is found between diabetics ≤10 years duration and diabetics > 10 years duration. Severity of NPDR did not affect CCT in this study. However, diabetics with PDR showed a higher CCT than those without PDR. No statistically significant difference in CCT is found between male and female diabetics. Poor correlation was found between CCT and RBS, PPBS, HbA1C. Whereas, FBS showed a positive correlation with CCT.

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ANNEXURES

ETHICAL CLEARANCE CERTIFICATES

B.L.D.E (Deemed to be University)
SHRI.B.M.PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE
VIJAYAPUR – 586103

IEC/NO: 288/2018
17-11-2018

INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2018 at 03-15 PM scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.

Title : Comparative study of central corneal thickness in diabetics and no-diabetics using ultrasonic pachymeter.

Name of P.G. Student : Dr Chinnanagolla Viveknandini Reddy.
Department of Ophthalmology,

Name of Guide/Co-investigator: Dr.M.H.Patil, Professor of Ophthalmology,

DR RAGHAVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College, VIJAYAPUR-586103.

Following documents were placed before E.C. for Scrutinization:

1) Copy of Synopsis/Research Project
2) Copy of informed consent form.
3) Any other relevant documents.

STUDY SUBJECT CONSENT FORM

I confirm that Dr. Chinnangolla Viveknandini Reddy has explained to me the purpose of research, the study procedure and the possible discomforts as well as benefits that I may experience in my own language. I have been explained all the above in detail in my own language and I understand the same. Therefore, I agree to give consent to participate as a subject in this research project.

_____ _____

(participant) (date)

_____ _____

(witness to signature) (date)

RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomforts during the examination or during the treatment. The procedures of this study are not expected to exaggerate these feelings which are associated with the usual course of treatment.

BENEFITS:

I understand that my participation will help in the assessment of CCT in diabetics.

I understand and accept the risks, benefits and costs involved. I willingly give consent to take part in the study.

CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of hospital records and will be subject to the confidentiality.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs will be used only with special written permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask for more questions about the study to Dr.M.H. PATIL in the Department of Ophthalmology who will be available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation. A copy of this consent form will be given to me to keep for careful reading.

REFUSAL FOR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice. I also understand that Dr. Chinnangolla Viveknandini Reddy may terminate my participation in the study after she has explained the reasons for doing so.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in the study, if such injury were reported promptly, the appropriate treatment would be available to me. But no further compensation would be provided by the hospital. I understand that by my agreements to participate in this study and not waiving any of my legal rights.

_____ _ _____

(participant) (date)

I have explained to _____the purpose of the research, the procedures required and the possible risks to the best of my ability.

_____ _____

Dr. Chinnangolla Viveknandini Reddy Date

(Investigator)

PROFORMA FOR CASE TAKING

DEPARTMENT OF OPHTHALMOLOGY

B.L.D. E UNIVERSITY'S SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA-586103

A COMPARATIVE STUDY OF CENTRAL CORNEAL THICKNESS IN DIABETICS AND NON-DIABETICS USING ULTRASONIC PACHYMETER

- ☐ **DURATION OF DIABETES >10 YEARS**
- ☐ **DURATION OF DIABETES <10 YEARS**
- ☐ **NON-DIABETIC**

- **CASE NO:** **OPD/IPD NO:**
  DATE:
- **NAME:** **AGE:**
  SEX:
- **OCCUPATION:** **ADDRESS:**
- **KNOWN CASE OF TYPE 2 DM:** **YES / NO**
- **DURATION OF TYPE 2 DM:**
- **REGULAR FOLLOW-UPS:** **YES / NO**
- **ON REGULAR MEDICATION:** **YES / NO**
- **TREATMENT HISTORY:**

- **ANY OTHER RELATED COMPLICATIONS:**

- **ANY OCULAR COMPLAINTS:**
- **PERSONAL HISTORY:**
- **PAST MEDICAL HISTORY:**

- **PAST SURGICAL HISTORY:**

- **FAMILY HISTORY:**

OPHTHALMIC EXAMINATION

	RIGHT EYE	LEFT EYE
External Appearance		
Ocular Motility		
Lids		
Conjunctiva		
Sclera		
Cornea		
Anterior Chamber		
Iris		
Pupil		
Lens		
Vision		
Unaided		
BCVA		
Near Vision		

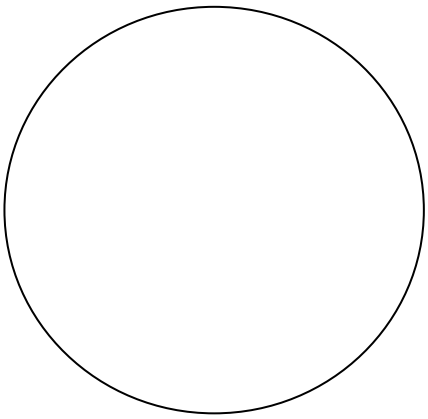
Central Corneal Thickness measurement by Ultrasonic Pachymeter

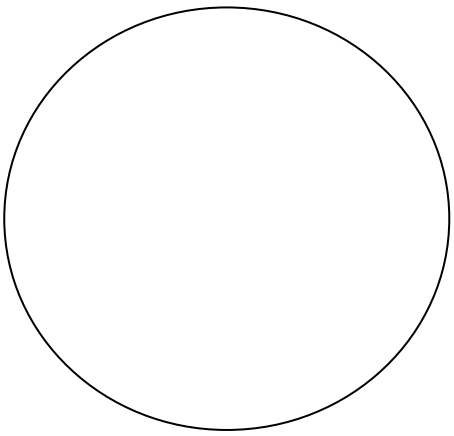
	RIGHT EYE	LEFT EYE
CCT (AVERAGE) in		

microns		

FUNDUS EXAMINATION

	RIGHT EYE	LEFT EYE
Media		
Disc		
Blood vessels		
Background		
Macula		

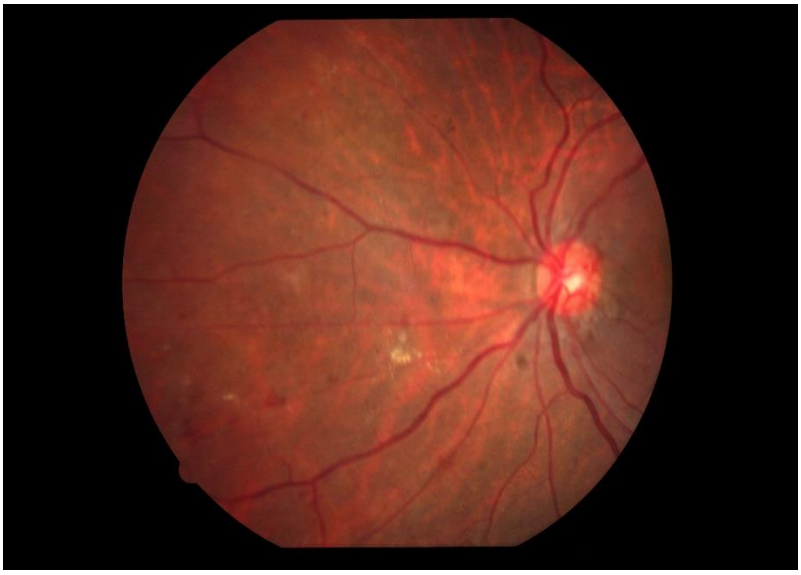


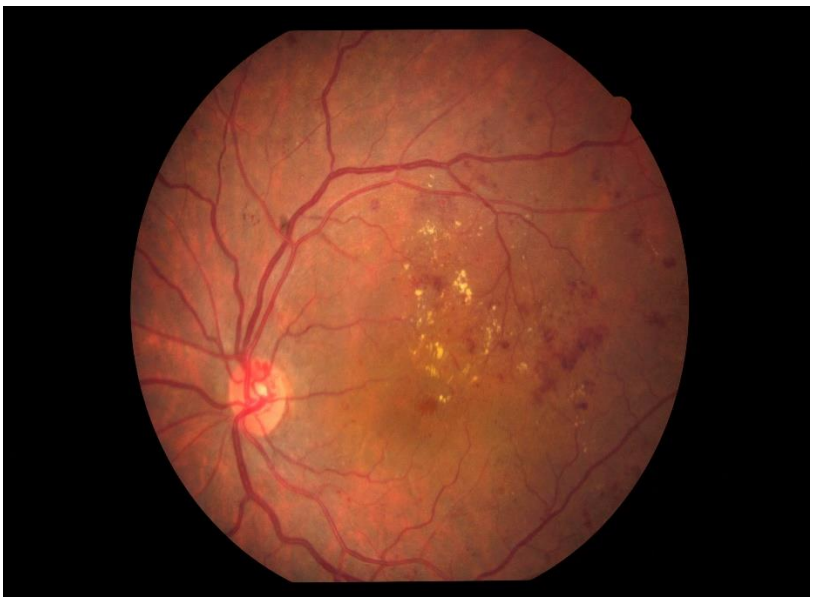


COLOR PLATES

Detailed slit lamp examination

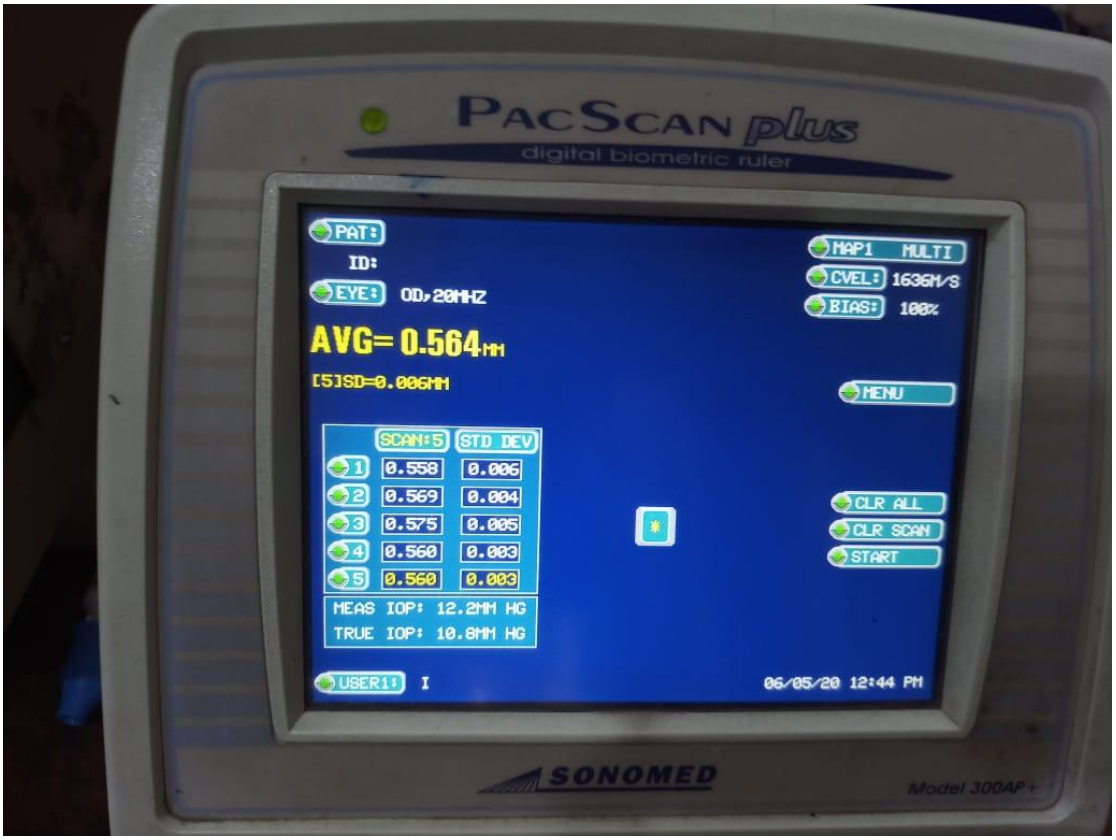
Indirect ophthalmoscopy





Fundus photograph of a diabetic patient.

Measuring CCT by Ultrasound Pachymetry



CCT in a patient with PDR

KEY TO MASTER CHART

S. No – Serial Number

OP No. – Outpatient department number

IP No. – Inpatient department number

F – Female

M – Male

T2DM – Type 2 Diabetes Mellitus

REG – Regular

F/U – Follow ups

Rx – Treatment

RBS – Random Blood Sugar

FBS – Fasting Blood Sugar

PPBS – Post Prandial Blood Sugar

CCT – Central corneal thickness

RE – Right Eye

LE – Left Eye

BE – Both eyes

V/A – visual acuity

BCVA – Best corrected visual acuity

CF – counting fingers

HM – Hand movements

NI – No improvement

PL – Perception of light

IOP – Intraocular pressure

NR – No retinopathy

NPDR – Non proliferative diabetic retinopathy

PDR – Proliferative diabetic retinopathy

MASTER CHART

S.No	OP/IP No	NAME	AGE(yrs)	SEX	DIABETIC	DURATION OF T2DM		REG F/U	REG Rx	RBS	FBS	PPBS	HbA1C	CCT		V/A		BVCA		IOP (corrected)		FUNDUS		OTHER COMPLICATIONS
						<10YEARS	>10YEARS							RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	
1	37038	Davalima Mulla	60	F	NO	_	_	_	_	86	_	_	_	478	480	6/24.	6/60.	6/18.	6/36.	12	14	NR	NR	NIL
2	37030	Parubai Tulajaram	75	F	NO	_	_	_	_	81	_	_	_	483	499	HMs	CF-2mts	NI	NI	12	12	NV	NV	NIL
3	37062	Shivappa Siddappa	61	M	NO	_	_	_	_	121	_	_	_	484	501	6/18.	6/12.	6/12.	6/9p	14	14	NR	NR	NIL
4	37058	Motilal Vachu	54	M	NO	_	_	_	_	104	_	_	_	489	488	6/18p	6/18.	6/9p	6/9.	12	12	NR	NR	NIL
5	37054	Bhimawwa Yankanna	70	F	NO	_	_	_	_	79	_	_	_	490	504	CF-1mt	CF-2mts	NI	NI	16	18	HAZY MEDIA(BE)		NIL
6	37047	Shantabai Nagyya	70	F	NO	_	_	_	_	111	_	_	_	494	501	CF-CF	CF-3mts	NI	NI	12	12	NV	HAZY	NIL
7	37066	Ratnabai Mulu	65	F	NO	_	_	_	_	143	_	_	_	496	486	6/60.	6/36p	6/36p	6/18p	12	12	NR	NR	NIL
8	37055	Siddamma Mahadev	58	F	NO	_	_	_	_	99	_	_	_	498	512	6/18p	6/24.	6/12.	6/12p	14	16	NR	NR	NIL
9	37049	Mahadevappa Gadad	75	M	NO	_	_	_	_	88	_	_	_	501	502	PL+ PR+	CF-1mt	NI	NI	14	14	NV	NV	NIL
10	37029	Girimalla Gadad	70	M	NO	_	_	_	_	78	_	_	_	501	504	CF-3mts	CF-3mts	NI	NI	18	18	NR	NR	NIL
11	37059	Dhansingh Shankar	48	M	NO	_	_	_	_	156	_	_	_	502	510	CF-CF	CF-3mts	NI	NI	16	16	NV	NR	NIL
12	37041	Basanna Ayyappa	74	M	NO	_	_	_	_	122	_	_	_	502	503	HMs	CF-2mts	NI	NI	20	20	NV	NR	NIL
13	37042	Jateppa Koragar	65	M	NO	_	_	_	_	104	_	_	_	502	508	6/24p	6/36.	6/18.	NI	18	16	NR	NR	NIL
14	37033	Chanaveerappa	65	M	NO	_	_	_	_	159	_	_	_	503	502	6/12p	6/9p	6/9p	6/9.	14	14	NR	NR	NIL
15	37051	Nilamma Ambyi	60	F	NO	_	_	_	_	100	_	_	_	503	505	6/36.	6/36.	6/24.	6/18p	12	12	NR	NR	NIL
16	37043	Gurubasamma	60	F	NO	_	_	_	_	171	_	_	_	504	508	6/18.	6/12.	6/12.	6/9p	14	14	NR	NR	NIL
17	37056	Devalabai Rathod	60	F	NO	_	_	_	_	86	_	_	_	505	511	6/24p	CF-5mts	6/12.	6/60.	12	12	NR	NR	NIL
18	37045	Shankrewwa Tuppad	53	F	NO	_	_	_	_	78	_	_	_	505	504	6/24.	6/12p	6/18.	6/9p	16	16	NR	NR	NIL
19	37064	Shankramma Devara	55	F	NO	_	_	_	_	180	_	_	_	507	505	6/60p	6/36p	6/36p	6/18p	12	12	NR	NR	NIL
20	37069	Shivasangappa	68	M	NO	_	_	_	_	120	_	_	_	509	511	CF-3mts	6/36p	NI	6/24.	14	12	NR	NR	NIL
21	37255	Sushilabai Badiger	50	F	NO	_	_	_	_	144	_	_	_	510	522	6/24p	6/36.	6/12.	6/12p	14	14	NR	NR	NIL
22	37316	Mahadevi Gadyal	50	F	NO	_	_	_	_	122	_	_	_	510	508	HMs	6/60.	NI	6/36.	12	12	NV	NR	NIL
23	4E+05	Kalavva	61	F	YES	YES	_	YES	YES	124	102	146	6.2	510	512	6/12.	6/12.	6/6.	6/6.	12	12	NR	NR	NIL
24	4E+05	P B Isaraddi	79	M	YES	_	YES	YES	YES	118	118	183	7	511	509	6/36p	6/36p	6/18p	6/18p	14	14	post laser status(BE)		NIL
25	3244	Sharanappa Kumbar	72	M	NO	_	_	_	_	71	_	_	_	511	510	6/24.	CF-3mts	6/12.	6/60.	16	12	NR	NR	NIL
26	3243	Bhimredddi	70	M	NO	_	_	_	_	90	_	_	_	511	512	CF-2mts	CF-3mts	NI	NI	16	14	NR	NR	NIL
27	3241	Ranganna Madar	70	M	NO	_	_	_	_	105	_	_	_	512	514	CF-1mt	CF-1mt	NI	NI	12	12	HAZY MEDIA(BE)		NIL
28	39260	Maleppa Badiger	53	M	YES	YES	_	YES	YES	156	124	199	6.9	513	498	6/6p	6/6.	6/6.	6/6.	16	16	NR	NR	NIL
29	4E+05	Laxmi Kuri	62	F	YES	YES	_	YES	YES	180	121	184	7.2	514	518	6/12.	6/12.	6/6.	6/6.	12	12	NR	NR	NIL

30	4E+05	Kalavva	61	F	YES	YES	_	YES	YES	122	100	199	7	514	515	6/12.	6/12.	6/6.	6/6.	18	16	NR	NR	NIL
31	4E+05	Sachidanand	52	M	YES	YES	_	YES	YES	199	125	189	7.2	514	515	6/6.	6/6.	6/6.	6/6.	20	22	PDR	PDR	NIL
32	4E+05	Hanamanth	55	M	YES	YES	_	YES	YES	81	81	168	6.5	515	515	6/24.	6/24.	6/6.	6/6.	14	14	NR	NR	NIL
33	38934	Sushila Biradar	50	F	YES	YES	_	YES	YES	198	125	187	7	517	517	6/24p	6/24.	6/9.	6/9.	14	12	NR	NR	NIL
34	41819	Dyamanna Takalaki	80	M	NO	_	_	_	_	85	_	_	_	518	519	CF-CF	CF-1mt	NI	NI	14	14	NV	HAZY	NIL
35	41810	Sonabai Takalakki	65	F	YES	YES	_	YES	YES	131	79	173	6.6	519	522	6/18.	6/12.	6/9p	6/6p	12	12	NR	NR	NIL
36	41821	Mahadevi Biradar	50	F	YES	_	YES	YES	YES	178	101	198	7	519	520	6/12.	6/9.	6/6.	6/6.	14	12	NR	NR	NIL
37	41767	Ningappa Pujari	65	M	NO	_	_	_	_	142	_	_	_	520	524	CF-3mts	6/36.	6/60.	6/24.	22	20	NR	NR	NIL
38	41983	Dhareppa Chabari	65	M	NO	_	_	_	_	167	_	_	_	520	519	6/12.	6/12.	6/9.	6/9.	12	10	NR	NR	NIL
39	42041	Siddanagouda	64	M	YES	_	YES	YES	YES	163	102	189	6.1	520	519	CF-2mts	6/60.	NI	6/24p	14	18	Mild NPDR (BE)		NIL
40	42044	Sabawwa Mulimani	69	F	NO	_	_	_	_	123	_	_	_	521	490	6/18.	6/18.	6/12.	6/12.	12	12	NR	NR	NIL
41	42042	Mallappa Hokkudi	62	M	YES	YES	_	YES	YES	121	77	132	6	521	520	6/12.	6/9.	6/9.	6/6.	10	12	NR	NR	NIL
42	42039	Mallamma Yalagi	65	F	NO	_	_	_	_	101	_	_	_	521	523									NIL
43	37036	ChandramSharanapa	72	M	NO	_	_	_	_	130	_	_	_	521	523	CF-3 mts	CF-3 mts	6/60.	6/60.	12	14	NR	NR	NIL
44	37032	Rukmabai Singh	60	F	NO	_	_	_	_	102	_	_	_	522	521	6/60.	6/36.	6/36.	6/18p	14	14	NR	NR	NIL
45	37050	Shattemma Shivanna	65	F	NO	_	_	_	_	85	_	_	_	522	522	CF-2 mts	6/18p	NI	6/12p	12	10	NR	NR	NIL
46	37065	Dundavva Ramanna	70	F	NO	_	_	_	_	92	_	_	_	523	526	CF-CF	CF-1mt	NI	NI	14	14	NV	HAZY	NIL
47	37048	Bhagappa Budihal	70	M	NO	_	_	_	_	112	_	_	_	524	518	6/36.	6/18p	6/24.	6/12.	12	12	NR	NR	NIL
48	37039	Sharanappa	65	M	NO	_	_	_	_	91	_	_	_	524	526	6/36.	6/60.	6/12p	6/24.	10	10	NR	NR	NIL
49	37061	Aminabai Bandagi	55	F	NO	_	_	_	_	106	_	_	_	524	528	6/24.	6/18p	6/18p	6/9p	12	12	NR	NR	NIL
50	37060	Fatima Ibransab	60	F	NO	_	_	_	_	80	_	_	_	524	523	6/9p	6/18.	6/6p	6/12.	14	14	NR	NR	NIL
51	37267	Irabasappa Harijan	75	M	NO	_	_	_	_	113	_	_	_	524	523	CF-3mts	6/60.	6/60.	6/18p	14	16	NR	NR	NIL
52	37317	Laxman Chandrappa	78	M	NO	_	_	_	_	93	_	_	_	525	522	HM+	CF-2 mts	NI	NI	20	18	HAZY	HAZY	NIL
53	37318	Siddappa Jijappa	70	M	NO	_	_	_	_	85	_	_	_	525	524	CF-3 mts	6/36.	NI	6/18p	14	14	NR	NR	NIL
54	37322	Gadigeppa	50	M	NO	_	_	_	_	92	_	_	_	525	527	6/36.	6/18p	6/12p	6/9p	12	12	NR	NR	NIL
55	38596	Sakkubai Rajaput	40	F	NO	_	_	_	_	192	_	_	_	525	524	6/12p	6/9p	6/6p	6/6.	12	12	NR	NR	NIL
56	38604	Lakshmibai Sidappa	60	F	NO	_	_	_	_	81	_	_	_	525	527	6/9p	6/6p	6/6p	6/6p	14	14	NR	NR	NIL
57	38660	Kamalabai Rathod	65	F	NO	_	_	_	_	79	_	_	_	526	530	6/12.	6/12p	6/9.	6/9.	16	16	NR	NR	NIL
58	38661	Shantamma	40	F	NO	_	_	_	_	81	_	_	_	526	526	6/6p	6/6.	6/6.	6/6.	10	10	NR	NR	NIL
59	38650	Akbar	67	M	NO	_	_	_	_	80	_	_	_	526	530	6/12p	6/9p	6/6p	6/6p	12	14	NR	NR	NIL
60	38655	Ramappa Bhilappa	66	M	NO	_	_	_	_	75	_	_	_	526	521	6/60.	6/18.	6/24p	6/12p	10	12	NR	NR	NIL
61	38869	Girimalla Shivagar	48	M	NO	_	_	_	_	89	_	_	_	526	525	6/6p	6/9p	6/6.	6/6.	14	14	NR	NR	NIL
62	38876	Shankar Rathod	70	M	NO	_	_	_	_	77	_	_	_	526	527	6/12.	CF-3 mts	6/9p	6/36p	12	16	NR	NR	NIL
63	38874	Mallanna Halli	70	M	NO	–	–	–	–	113	–	–	–	526	526	CF-2 mts	CF-1/2 mt	NI	NI	12	10	NR	HAZY	NIL
64	38864	Sharanagouda	57	M	NO	_	_	_	_	76	_	_	_	527	525	6/60.	6/18p	6/36.	6/12p	16	18	NR	NR	NIL
65	39445	Shantappa	63	M	NO	_	_	_	_	82	_	_	_	527	527	6/24.	6/12p	6/18.	6/9p	10	12	NR	NR	NIL

66	39457	Abdul Kasim	79	M	NO	–	–	–	–	120	–	–	–	527	527	CF-1/2 mt	CF-CF	NI	NI	14	18	NR	NV	NIL
67	39445	Shantappa Hedagi	63	M	NO	–	–	–	–	82	–	–	–	528	525	CF-1 mt	6/60.	NI	6/24.	12	12	NR	NR	NIL
68	39582	Siddamma Pujari	60	F	NO	–	–	–	–	120	–	–	–	528	530	CF- 2 mts	CF-3 mts	NI	6/60.	12	14	NR	NR	NIL
69	39841	Chandrappa	78	M	NO	–	–	–	–	90	–	–	–	528	527	6/36p	6/60.	6/24.	6/36p	10	10	NR	NR	NIL
70	39812	Basavaraj Chandappa	45	M	NO	–	–	–	–	104	–	–	–	528	530	6/6p	6/6.	6/6.	6/6.	20	20	NR	NR	NIL
71	39818	Jatteppa Ningappa	70	M	NO	–	–	–	–	88	–	–	–	528	527	CF-CF	PL+	NI	NI	12	12	NR	NV	NIL
72	39766	Amaramma Gollappa	70	F	NO	–	–	–	–	104	–	–	–	528	526	CF-3 mts	6/60.	NI	6/36.	14	16	NR	NR	NIL
73	39839	Guttamma Chandapa	67	F	NO	–	–	–	–	106	–	–	–	528	527	CF-1 mt	6/18p	NI	6/12.	18	14	NR	NR	NIL
74	39846	Basalingamma	60	F	NO	–	–	–	–	115	–	–	–	529	532	CF-2 mts	6/60.	NI	6/36p	16	12	NR	NR	NIL
75	40464	Lakkawwa Lakkappa	65	F	NO	–	–	–	–	116	–	–	–	529	526	6/36.	6/12p	6/24.	6/9p	14	14	NR	NR	NIL
76	40510	Channawwabasavant	68	F	NO	–	–	–	–	90	–	–	–	529	531	6/18p	6/12p	6/9p	6/6p	12	12	NR	NR	NIL
77	40500	Gangawwa Rangappa	55	F	NO	–	–	–	–	111	–	–	–	529	529	6/9p	6/12.	6/6p	6/6.	10	10	NR	NR	NIL
78	40563	Uddavva Sanakini	60	F	NO	–	–	–	–	85	–	–	–	530	529	6/12.	6/12.	6/6p	6/6.	12	12	NR	NR	NIL
79	40508	Shivayya Gurulingaya	74	M	NO	–	–	–	–	80	–	–	–	530	530	6/60.	6/36.	6/24p	6/18p	12	12	NR	NR	NIL
80	40503	Ramawwa Shivarudra	65	F	NO	–	–	–	–	79	–	–	–	530	531	6/9p	6/9.	6/6p	6/6p	14	14	NR	NR	NIL
81	40460	Siddawwa Lachappa	60	F	NO	–	–	–	–	113	–	–	–	531	532	6/12p	6/12.	6/9p	6/6p	18	16	NR	NR	NIL
82	40463	Kontewwa Sidapa	62	F	NO	–	–	–	–	117	–	–	–	531	540	6/9p	6/9p	6/6p	6/6.	14	16	NR	NR	NIL
83	39955	Sharanamma Pujari	55	F	NO	–	–	–	–	83	–	–	–	531	531	6/12.	6/24p	6/9p	6/18.	12	16	NR	NR	NIL
84	40467	Rama Tamanna	65	M	NO	–	–	–	–	113	–	–	–	531	532	CF-3 mts	6/60.	6/60.	6/24.	18	20	NR	NR	NIL
85	40468	Motiram Ramsingh	60	M	NO	–	–	–	–	123	–	–	–	531	531	6/36.	6/60.	6/24.	6/24p	12	10	NR	NR	NIL
86	42040	Shantabai Hippargi	67	F	NO	–	–	–	–	93	–	–	–	531	533	PL+	CF-2 mts	NI	NI	18	18	NV	HAZY	NIL
87	41779	Vimalabai	60	F	NO	–	–	–	–	104	–	–	–	532	530	6/9p	6/12p	6/9.	6/9.	12	12	NR	NR	NIL
88	42767	Basawwa Mallappa	70	F	NO	–	–	–	–	74	–	–	–	532	534	CF-1 mt	6/24.	NI	6/12p	14	12	HAZY	NR	NIL
89	42792	Nagawwa	65	F	NO	–	–	–	–	145	–	–	–	532	535	6/24p	6/18.	6/12p	6/12.	14	14	NR	NR	NIL
90	42794	Neelankant Shivappa	68	M	NO	–	–	–	–	88	–	–	–	532	535	6/36.	6/36.	6/18p	6/18.	18	14	NR	NR	NIL
91	42790	Chandrashekhar	62	M	NO	–	–	–	–	126	–	–	–	532	532	6/6p	6/12p	6/6.	6/12.	12	12	NR	NR	NIL
92	42791	Subhas Pawar	56	M	NO	–	–	–	–	106	–	–	–	532	530	6/12.	6/12.	6/6p	6/6.	12	12	NR	NR	NIL
93	42796	Appalal Hasanlal	48	M	NO	–	–	–	–	100	–	–	–	532	535	6/6p	6/6p	6/6.	6/6.	12	12	NR	NR	NIL
94	42045	Shankreppa	56	M	NO	–	–	–	–	88	–	–	–	532	533	6/12p	6/18p	6/6p	6/6p	10	10	NR	NR	NIL
95	4E+05	Anita Patil	52	F	YES	YES	–	YES	YES	199	123	177	6.2	533	531	6/12.	6/12.	6/6.	6/6.	10	12	Mild NPDR (BE)		NIL
96	37595	Irayya	84	M	YES	–	YES	YES	YES	187	120	187	7	533	538	CF 3mt	6/60.	6/60.	6/36p	14	12	NR	NR	NIL
97	37464	Bhimaray	55	M	YES	YES	–	YES	YES	171	89	142	6.9	533	538	6/9.	6/9.	6/6p	6/6.	16	16	NR	NR	NIL
98	4E+05	Gangavva	37	F	YES	YES	–	YES	YES	78	99	156	6.8	533	536	6/6.	6/6.	6/6.	6/6.	12	12	NR	NR	NIL
99	53632	Sachidanand	58	M	YES	–	YES	YES	YES	198	111	123	6.2	533	531	6/12.	6/9.	6/6p	6/6.	14	14	NR	NR	NIL
100	2894	Basamma	59	F	YES	YES	–	YES	YES	102	101	189	6.8	533	534	6/24.	6/12p	6/12.	6/9.	16	18	NR	NR	NIL
101	5E+05	Mallikarjun	49	M	YES	YES	–	YES	YES	156	116	199	7	534	536	6/12p	6/12.	6/6.	6/6.	16	16	Severe NPDR(BE)		NIL

102	2367	Mahadev	50	M	YES	_	YES	YES	YES	178	81	178	6.7	534	535	6/9.	6/6p	6/6.	6/6.	14	14	NR	NR	NIL
103	2208	Sonabai	60	F	YES	_	YES	YES	YES	143	99	120	5.8	534	531	6/18.	6/12.	6/12.	6/9p	10	10	NR	NR	NIL
104	2684	Shekar	65	M	YES	YES	_	YES	YES	123	107	119	5.7	535	537	6/60.	6/24.	6/24p	6/12p	12	12	NR	NR	NIL
105	32466	S.L.Kadani	79	M	YES	_	YES	YES	YES	154	125	157	7.1	535	537	CF 1mt	6/60.	NI	6/36p	14	14	NR	NR	NIL
106		Mahadev	70	M	YES	_	YES	YES	YES	99	100	192	6.1	535	534	6/36p	6/18p	6/24.	6/12p	12	12	Moderate NPDR(BE)		NIL
107	5E+05	Sharanath	61	M	YES	YES	_	YES	YES	100	119	166	5.9	535	539	6/18.	6/24.	6/9p	6/12p	14	14	Modertae NPDR(BE)		NIL
108	5E+05	Shivanand	63	M	YES	_	YES	YES	YES	177	109	151	7.2	536	537	6/60.	6/60.	6/36.	6/24p	12	12	NR	NR	NIL
109	5E+05	Rudrabar	65	M	YES	_	YES	YES	YES	152	79	176	7	536	539	6/9p	6/9.	6/6.	6/6.	14	14	NR	NR	NIL
110	5E+05	Parvati	65	F	YES	YES	_	YES	YES	158	97	152	7	536	536	6/24.	6/18.	6/12.	6/9p	12	12	NR	NR	NIL
111	5E+05	Sidagond	38	M	YES	_	YES	YES	YES	128	121	134	7.2	536	530	6/18p	6/18p	6/6.	6/6.	14	14	high risk PDR(BE)		NIL
112	42017	Basamma	55	F	YES	YES	_	YES	YES	180	120	154	5.4	537	536	6/9.	6/9.	6/6.	6/6.	16	16	Moderate NPDR(BE)		NIL
113	5E+05	Jogita	43	F	YES	YES	_	YES	YES	132	103	198	7.1	537	532	6/6.	6/6.	6/6p	6/6.	18	20	NR	NR	NIL
114	38934	Sushila	50	F	YES	_	YES	YES	YES	167	89	161	5.1	537	539	6/60.	6/60.	6/6.	6/6.	12	14	NR	NR	NIL
115	4E+05	Shoba	43	F	YES	YES	_	YES	YES	91	90	195	7	537	535	6/6.	6/6.	6/6.	6/6.	12	12	NR	NR	NIL
116	4E+05	Sangamesh	65	M	YES	_	YES	YES	YES	139	78	195	6.6	538	536	6/36.	6/36.	6/24p	6/18p	14	14	NR	NR	NIL
117	40992	Kasturibai	65	F	YES	_	YES	YES	YES	90	115	172	6	538	538	6/12.	6/12.	6/6p	6/6p	20	18	Moderate NPDR(BE)		NIL
118	39050	Mayawwa	65	F	YES	_	YES	YES	YES	129	117	170	5.8	538	536	6/9.	6/6p	6/6p	6/6.	12	12	NR	NR	NIL
119	39215	Chintamma	60	F	YES	YES	_	YES	YES	89	109	180	7.2	539	541	6/12.	6/12.	6/6.	6/6.	12	12	Moderate NPDR(BE)		NIL
120	39246	Gadigeppa	77	M	YES	_	YES	YES	YES	193	103	131	6.5	539	538	CF 2 mts	CF 3 mts	CF 3 mts	6/60.	10	10	NR	NR	NIL
121	4E+05	Hanamanth	63	M	YES	_	YES	YES	YES	89	111	128	6.1	539	537	CF 3mt	6/36.	CF 4mt	6/18p	18	18	NR	NR	NIL
122	38876	Sulochana	65	F	YES	_	YES	YES	YES	75	77	176	7.2	539	535	6/9p	6/6.	6/6.	6/6.	10	10	Mild NPDR (BE)		NIL
123	81476	Shantamma	60	F	YES	YES	_	YES	YES	86	95	196	7.1	539	537	CF 3mt	CF 3 mts	6/6p	6/6p	12	12	NR	NR	NIL
124	38234	Shreeshail	42	M	YES	_	YES	YES	YES	88	125	178	7	539	541	6/18p	6/18.	6/6.	6/6.	12	12	Severe NPDR(BE)		NIL
125	12816	Sadashiv	60	M	YES	_	_	YES	YES	190	121	145	7.2	540	542	6/18p	6/24.	6/12.	6/18.	12	12	Advanced PDR (BE)		NIL
126		Pramila	60	F	YES	YES	_	YES	YES	92	120	162	7	540	541	6/12.	6/12.	6/9.	6/9p	14	14	Mild NPDR (BE)		NIL
127	5E+05	Vijay Kumar	44	M	YES	YES	_	YES	YES	126	122	178	7.2	540	541	6/6.	6/6.	6/6.	6/6.	12	12	NR	NR	NIL
128	37427	Ramappa	60	M	YES	_	YES	YES	YES	145	117	154	5.5	540	542	6/12p	6/9p	6/6.	6/6.	10	10	NR	NR	NIL
129	42018	Narasappa	65	M	YES	YES	_	YES	YES	96	92	100	5.9	540	542	6/9.	6/9.	6/6.	6/6.	12	12	NR	NR	NIL
130	27524	Davalsab	57	M	YES	YES	_	YES	YES	131	102	128	6.4	541	534	6/18.	6/24.	6/9p	6/9.	12	12	NR	NR	NIL
131	8366	Chandabai	70	F	YES	_	YES	YES	YES	199	97	167	5	541	543	6/60.	CF 3 mts	6/36.	6/60.	12	12	Early PDR (BE)		NIL
132	42566	Basalingappa	55	M	YES	YES	_	YES	YES	94	99	148	5.9	542	537	6/18.	6/12.	6/12.	6/9.	10	10	NR	NR	NIL
133	5878	Indu	60	F	YES	_	YES	YES	YES	198	111	92	7	542	545	6/9.	6/9.	6/6p	6/6p	14	16	Moderate NPDR(BE)		NIL
134	5921	Arasgond	57	M	YES	YES	_	YES	YES	125	112	123	7.2	542	542	6/36.	6/36.	6/6p	6/6p	14	14	NR	NR	NIL
135	6438	Mohammed	63	M	YES	_	YES	YES	YES	160	111	180	6.4	543	547	6/12.	6/12.	6/9.	6/9.	12	12	Mild NPDR (BE)		NIL
136	70546	Vimala	57	F	YES	_	YES	YES	YES	79	116	149	6	543	541	6/12.	6/12.	6/6.	6/6.	12	12	Early PDR (BE)		NIL
137	27549	Parameshwar	57	M	YES	YES	_	YES	YES	169	92	150	6.7	543	544	6/18.	6/24.	6/12.	6/12p	10	10	NR	NR	NIL

138	42552	Sangavva	60	F	YES	YES	_	YES	YES	111	95	177	7.2	543	542	6/12.	6/12.	6/9.	6/9p	14	14	Mild NPDR (BE)		NIL	
139	4E+05	Ravi	43	M	YES	_	YES	YES	YES	109	98	145	5	544	545	6/6.	6/6.	6/6.	6/6.	16	16	Moderate NPDR(BE)		NIL	
140	31825	Shekawwa	60	F	YES	YES	_	YES	YES	104	79	167	5.8	544	548	6/24.	6/36.	6/12p	6/24.	12	12	NR	NR	NIL	
141	27526	Rewanawwa	69	F	YES	_	YES	YES	YES	75	78	139	6.3	544	542	6/18p	6/60.	6/12.	6/36.	12	12	NR	NR	NIL	
142	42542	Billu	65	M	YES	_	YES	YES	YES	100	114	160	5.4	545	547	6/12.	6/9.	6/6p	6/6.	14	14	Moderate NPDR(BE)		NIL	
143	6285	Sabawwa	55	F	YES	YES	_	YES	YES	96	96	148	6	546	544	6/36.	6/36.	6/6.	6/6.	14	14	Severe PDR (BE)		NIL	
144	12773	Girimalla	60	M	YES	_	YES	YES	YES	101	117	159	6.6	546	547	6/36.	6/36.	6/9p	6/9.	12	16	PDR (BE) with RD(RE)		NIL	
145	12726	Mashaque	65	M	YES	_	YES	YES	YES	129	119	181	6.7	546	545	6/9p	6/12.	6/6p	6/6p	12	12	Severe NPDR(BE)		NIL	
146	12789	Mallaappa	72	M	YES	_	YES	YES	YES	129	102	199	7.2	546	544	CF 1 mt	6/60.	CF 3 mts	6/36.	12	12	High risk PDR (BE)		NIL	
147	13360	Sharanappa	45	M	YES	YES	_	YES	YES	76	120	194	7.1	546	546	6/12.	6/9.	6/6.	6/6.	12	12	NR	NR	NIL	
148	13022	Guraling	60	M	YES	YES	_	YES	YES	198	61	150	6.8	547	546	6/60.	6/36.	6/24p	6/18p	14	12	High risk PDR (BE)		NIL	
149	1E+05	Kallappa	65	M	YES	YES	_	YES	YES	90	115	168	6.4	547	548	6/9.	6/9.	6/6p	6/6p	16	16	NR	NR	NIL	
150	14007	Krishnappa	64	M	YES	YES	_	YES	YES	170	98	180	5.6	547	545	6/12.	6/9.	6/9.	6/6p	22	20	NR	NR	NIL	
151	14013	Kallappa	55	M	YES	YES	_	YES	YES	123	93	167	7	547	546	6/9.	6/6p	6/6p	6/6.	14	12	NR	NR	NIL	
152	1E+05	Suresh Chavan	46	M	YES	YES	_	YES	YES	134	79	147	7.2	548	546	6/6.	6/6.	6/6.	6/6.	12	14	NR	NR	NIL	
153	1E+05	Kasturi	62	F	YES	YES	_	YES	YES	125	104	136	6	549	549	6/12.	6/12.	6/9p	6/9p	12	12	NR	NR	NIL	
154	1E+05	Maibibasab	60	M	YES	_	YES	YES	YES	198	86	197	6.2	549	550	6/12.	6/9p	6/9.	6/9.	14	14	Moderate NPDR(BE)		NIL	
155	13946	Shajeet	62	M	YES	_	YES	YES	YES	189	121	182	5.7	549	546	6/9.	6/12.	6/6p	6/9p	18	18	Moderate NPDR(BE)		NIL	
156	14366	Mahantesh	38	M	YES	YES	_	YES	YES	100	121	174	6.5	549	550	6/6.	6/6.	6/6.	6/6.	12	12	NR	NR	NIL	
157	14485	Sumangala	61	F	YES	_	YES	YES	YES	139	102	176	5.9	550	548	6/12.	6/12.	6/9p	6/9.	14	14	Mild NPDR (BE)		NIL	
158	14530	Ningappa	65	M	YES	YES	_	YES	YES	157	120	199	6	554	556	6/12.	6/12.	6/6p	6/6p	10	10	NR	NR	NIL	
159	14497	Sudram	45	M	YES	_	YES	YES	YES	199	108	167	7.1	554	558	CF 3 mts	6/60.	NI	6/36p	14	10	PDR (BE)		NIL	
160	14861	Gangavva	60	F	YES	_	YES	YES	YES	119	102	198	5.9	555	558	6/24.	6/18.	6/12p	6/12.	12	10	Moderate NPDR(BE)		NIL	
161	14995	Shanmukappa	69	M	YES	_	YES	YES	YES	111	101	170	6.1	563	565	CF 3mt	CF 2mts	6/60.	CF 3mt	14	14	Moderate NPDR(BE)		NIL	
162	15469	Ramjan	38	M	YES	YES	_	YES	YES	80	124	159	6.4	565	564	6/9.	6/9.	6/6.	6/6.	12	12	Moderate NPDR(BE)		NIL	
163	37459	Noorjahan	49	F	YES	_	YES	YES	YES	107	105	154	5.8	568	571	6/6.	6/6.	6/6.	6/6.	10	10	NR	NR	NIL	
164	15404	Rudragouda	65	M	YES	YES	_	YES	YES	156	116	41	5.8	569	566	6/18.	6/12.	6/9.	6/9p	10	12	Mild NPDR (BE)		NIL	
165	15250	Sharanagoud	69	M	YES	_	YES	YES	YES	180	99	132	4.9	571	569	CF 1mt	CF 3 mts	NI	6/36p	10	12	NR	NR	NIL	
166	36514	Dilip	45	M	YES	YES	_	YES	YES	123	109	178	5.9	580	581	6/9.	6/9.	6/6.	6/6.	10	12	NR	NR	NIL	
167	36503	Irayya	60	M	YES	YES	_	YES	YES	125	98	198	5	587	584	6/12.	6/12.	6/6.	6/6.	12	10	NR	NR	NIL	
168	15482	Suvarna	49	F	YES	_	YES	YES	YES	114	105	156	5.6	598	596	6/9.	6/9p	6/6.	6/6.	12	12	Moderate NPDR(BE)		NIL	