"RETINAL FINDINGS IN DIABETIC CHRONIC KIDNEY DISEASE PATIENTS AND NON - DIABETIC CHRONIC KIDNEY DISEASE PATIENTS: A COMPARATIVE STUDY."

By

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Dissertation submitted to the

B.L.D.E. (DEEMED TO BE UNIVERSITY)

VIJAYAPURA, KARNATAKA

In Partial fulfilment of requirements for the degree of

MASTER OF SURGERY

In

OPHTHALMOLOGY

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ACKNOWLEDGEMENT

With a humble heart, I would like to begin this acknowledgement with a prayer to the Almighty God, who has given us the strength, wisdom, and grace to embark on this scholarly journey.

I am profoundly grateful to my teacher, mentor and guide, ***Prof. (Dr.) RAGHAVENDRA. K. IJERI****, whose unwavering inspiration, encouragement, and support have been instrumental throughout my post-graduation studies and the preparation of my dissertation. Her guidance has been invaluable, and I deeply appreciate her dedication to my academic and professional growth.*

I am deeply indebted to my esteemed Professors, ***Dr. Rekha R Mudhol****,* ***Dr. Sunil Biradar*** *and* ***Dr Vallabha K,*** *as well as my Professor****, Dr. Raghavendra K Ijeri****, whose guidance and encouragement have propelled me to new heights of professional achievement throughout my course. Their mentorship has been instrumental in shaping my academic journey, and I am forever grateful for their invaluable support and inspiration.*

My heartfelt thanks and deep gratitude to my teachers, ***Dr. Keerti Wali, Dr. Talluru Subash, Dr. Shweta Patil, Dr. Magna Mary*** *and* ***Dr. Suman D****. Without their inspiration, timely guidance, immense support, and motivation, I wouldn't have been able to complete this dissertation.*

I am grateful to ***Dr. Aravind V Patil****, Principal of BLDE (DU) 's Shri B. M Patil Medical College Hospital and Research Centre, Vijayapura, for permitting me to utilise the resources in the completion of my work. I am extremely thankful*

*to **Dr. Vijaya Sorganvi** for her guidance in statistical analysis. I thank my friends and colleagues specially **Dr. Vaishnavi Patil** and **Dr. Shilpa K.** for their constant support.*

*I express my heartfelt appreciation and gratitude to my beloved parents, **Mr. Rajesh C Gandhi** and **Dr. Mrs. Soniya R Gandhi,** and my beloved brother **Sanat Gandhi** for their support, invaluable advice, and endless encouragement. Their boundless love and sacrifices have been the cornerstone of my journey, and I am deeply indebted to them for instilling in me the values of perseverance and determination.*

Finally, I acknowledge my heartfelt gratitude to all my patients; this study would be incomplete without their participation.

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LIST OF ABBREVIATIONS

Abbreviation	Full Form
CKD	Chronic Kidney Disease
D-CKD	Diabetic Chronic Kidney Disease
ND-CKD	Non-Diabetic Chronic Kidney Disease
DM	Diabetes Mellitus
DR	Diabetic Retinopathy
NPDR	Non-Proliferative Diabetic Retinopathy
PDR	Proliferative Diabetic Retinopathy
SD-OCT	Spectral-Domain Optical Coherence Tomography
OCT	Optical Coherence Tomography
CST	Central Subfield Thickness
pRNFL	Peripapillary Retinal Nerve Fiber Layer
RAAS	Renin-Angiotensin-Aldosterone System
RPE	Retinal Pigment Epithelium
eGFR	Estimated Glomerular Filtration Rate

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ABSTRACT

Introduction:

Chronic kidney disease (CKD) is a progressive multisystemic disorder with significant microvascular complications. The retina, due to its embryological and physiological similarity to renal vasculature, reflects systemic vascular changes, particularly in diabetic chronic kidney disease (D-CKD). This study aimed to compare retinal structural and vascular alterations in patients with D-CKD and non-diabetic CKD (ND-CKD), utilizing spectral-domain optical coherence tomography (SD-OCT) and fundus examination to determine the extent of microangiopathy across groups and its correlation with renal parameters.

Methods:

A cross-sectional comparative study was conducted on 76 CKD patients (38 D-CKD and 38 ND-CKD) at a tertiary care hospital in Karnataka, India. All subjects underwent detailed ophthalmological evaluation including best-corrected visual acuity, intraocular pressure measurement, slit-lamp biomicroscopy, fundus photography, and SD-OCT imaging. Retinal thickness parameters were analyzed across five quadrants. Renal function was assessed using serum creatinine and estimated glomerular filtration rate (eGFR) via the Cockcroft-Gault formula. Fundus findings were classified according to standard retinopathy grading systems. Statistical comparisons were made using t-tests, chi-square, and correlation analyses.

Results:

D-CKD patients demonstrated significantly greater retinal thinning across all macular quadrants ($p<0.001$), with mean subfoveal thickness of 220.11 ± 39.67 μm (RE) versus 265.50 ± 28.34 μm in ND-CKD. Proliferative and non-proliferative diabetic retinopathy were exclusive to the D-CKD group, while hypertensive retinopathy was more common in ND-CKD. A strong inverse correlation was observed between eGFR and retinal thinning ($r = -0.65$, $p<0.01$). Patients on dialysis exhibited more severe OCT and fundus abnormalities. Among ND-CKD etiologies, hypertensive nephropathy was most associated with retinal microvascular signs.

Conclusion:

Retinal changes in CKD reflect systemic microvascular pathology, with diabetic CKD demonstrating more advanced alterations due to synergistic effects of hyperglycemia and uremia. SD-OCT provides a sensitive

modality for detecting early neuroretinal damage. Routine retinal imaging may aid in risk stratification, progression monitoring, and interdisciplinary care planning in CKD patients. This study underscores the value of ophthalmic surveillance in nephrology protocols.

INTRODUCTION

Chronic kidney disease (CKD) is a **global public health challenge** with an estimated prevalence of **9.1%**, affecting approximately **700 million individuals worldwide**, and accounting for **1.2 million deaths annually** [1]. CKD represents the **11th leading cause of death globally** and is projected to become the **5th leading cause of mortality** by **2040** [2]. The disease burden is not uniformly distributed, with **developing countries** like **India** carrying a disproportionate share of cases due to the increasing prevalence of **diabetes mellitus (DM)** and **hypertension**, which are the primary risk factors for CKD [3]. In India, the prevalence of CKD is estimated to be **17.2%**, with nearly **6% of the population** suffering from advanced stages of CKD [4]. Within the state of **Karnataka**, data indicate a rising burden of CKD, largely attributed to **poorly managed diabetes**, **hypertension**, and **chronic glomerulonephritis**, with estimated prevalence rates of **15-20%** among high-risk populations [5].

The growing epidemic of **CKD in India** reflects a combination of **demographic transition**, **urbanization**, and **lifestyle-related factors**, with **diabetic kidney disease (DKD)** accounting for **40-50% of cases** [6]. As of 2021, diabetes and hypertension contribute to **nearly 60% of CKD cases** in urban populations and **50% in rural areas** [7]. Moreover, the prevalence of **end-stage renal disease (ESRD)**, the most advanced stage of CKD, has shown a sharp rise, with **220–250 new ESRD cases per million population annually**, placing a heavy burden on the healthcare infrastructure [8].

The **retina**, being **highly vascularized**, serves as a **window to systemic vascular health**, making it an important tool for evaluating microvascular changes in CKD. Both the **retina and kidneys** share similar **microvascular structures** and are affected by **common pathophysiological mechanisms** such as **endothelial dysfunction**, **oxidative stress**, and the **renin-angiotensin-aldosterone system (RAAS)** [9]. Retinal microvascular changes, such as

arteriolar narrowing, **venular dilatation**, **microaneurysms**, and **hard exudates**, have been well-documented in CKD patients, particularly in those with **diabetes** [10]. These findings provide valuable insights into systemic vascular health and are non-invasive compared to conventional diagnostic tools.

Diabetic chronic kidney disease (D-CKD) is a major contributor to the **global burden of CKD**, accounting for nearly **40% of all CKD cases worldwide** [11]. In India, the prevalence of **diabetic nephropathy** is estimated at **30-40% among individuals with diabetes**, making it the leading cause of CKD [12]. Karnataka, reflecting national trends, reports a high prevalence of D-CKD, with nearly **35-45% of CKD cases** attributed to poorly controlled diabetes and associated complications [13]. A study conducted in Bengaluru found that **over 50% of CKD patients** had diabetes as the primary etiology, underscoring the importance of integrated diabetes and CKD management in the state [14].

While **non-diabetic CKD (ND-CKD)** encompasses a wide range of etiologies such as **hypertensive nephropathy**, **glomerulonephritis**, and **polycystic kidney disease**, its contribution to the global CKD burden is also significant, particularly in rural and resource-limited settings. Worldwide, ND-CKD accounts for approximately **60% of CKD cases**, with hypertension being the leading cause in **developed nations**, while **chronic infections** and **toxin exposure** are major contributors in **developing countries** [15]. In India, ND-CKD is more prevalent in rural areas, where **hypertension**, **chronic glomerulonephritis**, and **undiagnosed infections** are common causes, contributing to nearly **50% of CKD cases in these regions** [16]. In Karnataka, a study conducted in rural populations revealed a prevalence of **15-20% for ND-CKD**, with a significant proportion of cases attributable to **hypertension** and **undiagnosed renal conditions** [17].

The retina offers a unique platform for evaluating the systemic vascular effects of CKD. Retinal findings, including **macular thinning**, **choroidal changes**, and **peripapillary retinal nerve fiber layer (pRNFL) thinning**, correlate with CKD progression and provide valuable diagnostic and prognostic information [(18).] Advanced imaging techniques such as **spectral-domain optical coherence tomography (SD-OCT)** and **optical coherence tomography angiography (OCTA)** have emerged as non-invasive tools to assess these changes. Studies have shown that retinal imaging can detect microvascular abnormalities even in early stages of CKD, offering an opportunity for **early intervention** [(19).]

The rising burden of **CKD worldwide**, especially in **India** and **Karnataka**, underscores the need for innovative diagnostic and management strategies. By comparing **retinal findings** in diabetic and non-diabetic CKD patients, this study aims to unravel distinct and overlapping mechanisms underlying systemic microvascular dysfunction. Such findings could pave the way for **integrated care models** that leverage retinal imaging as a non-invasive biomarker for CKD, improving early detection and management in high-risk populations.

AIM AND OBJECTIVES

Aim:

To study the retinal findings of diabetic chronic kidney disease patients and that of non-diabetic chronic kidney disease patients.

Objectives:

1] To compare the retinal findings in patients of diabetic chronic kidney disease with that of non-diabetic chronic kidney disease.

2] To study the retinal findings in various non-diabetic causes of chronic kidney disease.

REVIEW OF LITERATURE

The **KDIGO 2024 definition of chronic kidney disease (CKD)** emphasizes the importance of sustained abnormalities in kidney structure or function that persist for over three months and have significant implications for overall health. This definition encompasses a broad range of markers, including a **glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m²** and **markers of kidney damage** such as **albuminuria**, structural abnormalities, or other indicators detected through imaging or laboratory tests. By incorporating both functional and structural criteria, this definition highlights CKD as a long-term, progressive condition that impacts systemic health, including **microvascular complications in the retina**, necessitating early detection, comprehensive evaluation, and ongoing management to mitigate complications and improve patient outcomes.

1. Epidemiology of Chronic Kidney Disease (CKD)

CKD is recognized as a major public health concern worldwide, with a prevalence of **9.1% globally** and an estimated **1.2 million deaths annually** [(1)]. The increasing prevalence of CKD is particularly evident in low- and middle-income countries like India, where the prevalence is **17.2%** [(2)]. Diabetic kidney disease (DKD) accounts for **40-50% of CKD cases**, making it the leading cause of CKD [(3)]. In India, urban studies indicate that diabetes and hypertension contribute to **60% of CKD cases**, while rural studies reveal that chronic infections and undiagnosed nephropathies contribute significantly to **non-diabetic CKD (ND-CKD)** [(4)].

2. Pathophysiology of Retinal and Renal Microvascular Changes

The **retina** and the **kidneys** share a similar microvascular structure and pathophysiological mechanisms, which explains their systemic connection in conditions like **chronic kidney disease (CKD)**. Both organs rely on intact microvascular networks to maintain their function, and damage to these networks can lead to **retinopathy** in the eye and **nephropathy** in the kidney. The major mechanisms involved in this pathological process include **oxidative stress**, **chronic inflammation**, **endothelial dysfunction**, and **activation of the renin-angiotensin-aldosterone system (RAAS)**, all of which collectively contribute to the microvascular damage observed in CKD.

1) Oxidative Stress

i) **Oxidative stress** is one of the key mechanisms driving microvascular damage in both the retina and kidneys. In CKD, excessive production of **reactive oxygen species (ROS)** overwhelms the body's antioxidant defenses, leading to **oxidative damage** in endothelial cells and microvascular tissues. This is particularly relevant in diabetic CKD (D-CKD), where chronic hyperglycemia exacerbates ROS production through pathways such as the **polyol pathway**, **protein kinase C activation**, and the formation of **advanced glycation end products (AGEs)**. In the retina, oxidative stress leads to endothelial injury, which contributes to **increased vascular permeability**, **ischemia**, and the development of characteristic retinal findings such as **micro-aneurysms** and **cotton wool spots**. In CKD, oxidative stress also accelerates renal tubular damage, leading to fibrosis and a decline in glomerular filtration rate [1, 2]. Studies have shown that markers of oxidative stress, such as **malondialdehyde**, are elevated in both CKD and diabetic retinopathy patients, highlighting the shared mechanism [3].

2) Chronic Inflammation

i) **Chronic inflammation** is a hallmark of both CKD and retinal microvascular damage. In CKD, a pro-inflammatory state is induced due to the retention of **uremic toxins**, activation of immune pathways, and persistent low-grade infection. Pro-inflammatory cytokines such as **interleukin-6 (IL-6)**, **tumor necrosis factor-alpha (TNF-α)**, and **C-reactive protein (CRP)** are elevated in CKD patients, promoting endothelial damage and vascular remodeling. In the retina, inflammation leads to the release of **vascular endothelial growth factor (VEGF)**, which exacerbates vascular permeability and neovascularization. These processes result in retinal findings such as **macular edema** and **neovascularization**, particularly in diabetic retinopathy [(4).] In non-diabetic CKD (ND-CKD), inflammation also drives microvascular changes, though without the direct effects of hyperglycemia, making the damage subtler but still significant.

3) Endothelial Dysfunction

i) **Endothelial dysfunction** is a critical mechanism linking CKD and retinal microvascular damage. The endothelium regulates vascular tone, permeability, and blood flow. In CKD, **uremic toxins** such as **indoxyl sulfate** and **p-cresyl sulfate** impair endothelial function by reducing the availability of **nitric oxide (NO)**, a key vasodilator. This leads to **vasoconstriction**, **ischemia**, and increased vascular stiffness. Endothelial dysfunction is further aggravated in D-CKD by hyperglycemia and AGEs, resulting in capillary leakage and **vascular rarefaction** in both the retina and kidneys [(5)]. In the retina, these changes manifest as **cotton wool spots**, **venular dilatation**, and **hard exudates**. A study involving CKD patients demonstrated a strong association between reduced NO

bioavailability and the presence of retinal microvascular changes, emphasizing the systemic nature of endothelial dysfunction [6].

4) **Activation of the Renin-Angiotensin-Aldosterone System (RAAS)**

   i) The **renin-angiotensin-aldosterone system (RAAS)** plays a pivotal role in regulating blood pressure and fluid balance, but its over-activation in CKD contributes to widespread microvascular damage. Elevated levels of **angiotensin II** promote **vasoconstriction**, **endothelial injury**, and **fibrosis**. In the retina, RAAS activation is associated with **arteriolar narrowing**, **venular dilatation**, and **increased VEGF expression**, leading to pathological changes such as **neovascularization** in advanced stages of retinopathy. In CKD, the same mechanisms contribute to glomerular hypertension, proteinuria, and progressive kidney damage [7]. Clinical studies have shown that RAAS inhibitors, such as **angiotensin-converting enzyme (ACE) inhibitors** and **angiotensin receptor blockers (ARBs)**, can reduce the progression of both retinopathy and nephropathy by mitigating oxidative stress, inflammation, and VEGF overexpression [8].

5) Retinal Microvascular Changes in CKD

The pathophysiological processes outlined above culminate in specific retinal microvascular changes that mirror the systemic vascular damage seen in CKD. These include:

Arteriolar narrowing: Due to chronic vasoconstriction and vascular remodeling, resulting in reduced oxygen delivery to retinal tissues.

Venular dilatation: Reflecting increased venous pressure and endothelial dysfunction.

Microaneurysms: Caused by weakened vascular walls and increased permeability.

Cotton wool spots: Indicative of retinal ischemia and microvascular occlusion.

Macular edema and hard exudates: Reflecting leakage of plasma proteins and lipids due to vascular permeability [9].

A large-scale study of **7,228 participants** without diabetes found that retinopathy signs, such as microaneurysms and venular dilatation, were present in **25-30% of CKD patients**, underscoring the systemic vascular involvement in CKD [10]. These findings were more severe in D-CKD patients due to the combined effects of hyperglycemia and CKD-related vascular dysfunction.

3. Retinal Findings in Diabetic Chronic Kidney Disease (D-CKD)

Diabetic chronic kidney disease (D-CKD) is associated with distinct retinal abnormalities due to the combined effects of **hyperglycemia**, **hypertension**, and **microvascular complications**. The interplay between systemic vascular dysfunction and localized retinal damage leads to several characteristic retinal findings in D-CKD.

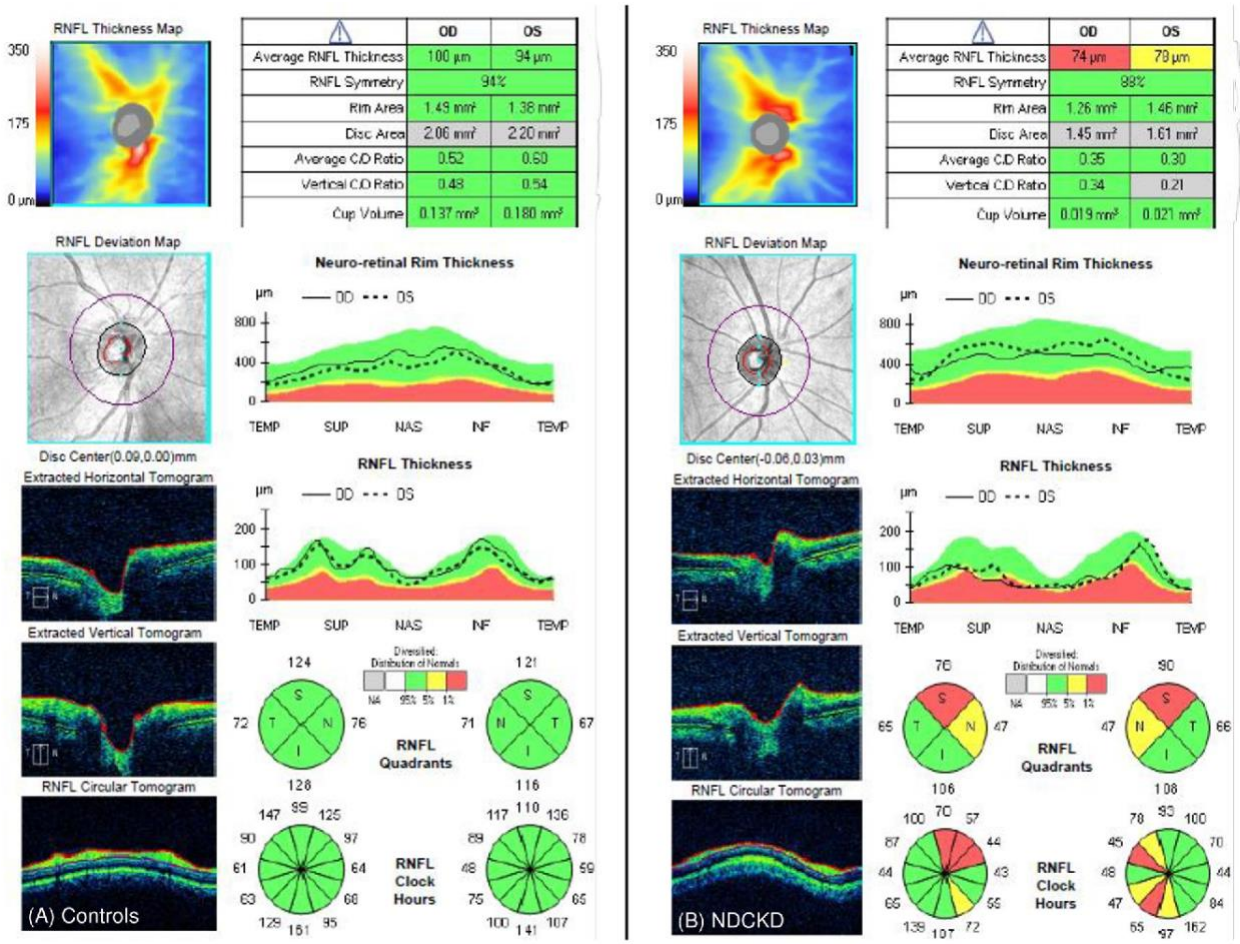


Fig 1. OCT image of pRNFL thickness measurement for controls and NDCKD group. (A) Control group (B) NDCKD group. Abbreviation:

Figure 1. OCT image of pRNFL thickness measurement for controls and NDCKD group. (A) Control group (B) NDCKD group. Abbreviation: pRNFL = peripapillary retinal nerve fiber layer; NDCKD = non-diabetic chronic kidney disease

1. **Diabetic Retinopathy (DR):**

Diabetic retinopathy is present in up to **95% of patients with D-CKD**. It represents a spectrum of retinal changes ranging from **non-proliferative diabetic retinopathy (NPDR)**, characterized by microaneurysms, intraretinal hemorrhages, and hard exudates, to **proliferative diabetic retinopathy (PDR)** with neovascularization and vitreous hemorrhage [(1).] The development of DR is driven by hyperglycemia-induced oxidative stress, endothelial dysfunction, and

the upregulation of vascular endothelial growth factor (VEGF) [2]. Studies have shown that the **severity of DR correlates with CKD progression**, suggesting a shared pathophysiological pathway between the two conditions [3].

2. **Choroidal Thinning:**

   Structural changes in the **choroid**, as assessed by **spectral-domain optical coherence tomography (SD-OCT)**, reveal significant thinning in D-CKD patients. The choroid is essential for retinal health as it supplies oxygen and nutrients to the outer retina. Hyperglycemia-induced ischemia and VEGF overexpression lead to choroidal thinning, which is more pronounced in advanced stages of diabetic nephropathy [4]. A study by Da Silva et al. demonstrated that **choroidal thinning** was significantly associated with **reduced estimated glomerular filtration rate (eGFR)** in diabetic CKD patients [5].

3. **Macular Edema:**

   Macular edema, a hallmark of advanced diabetic retinopathy, is commonly observed in D-CKD patients. It results from **increased vascular permeability** caused by endothelial dysfunction and VEGF overexpression (6). Macular edema contributes significantly to **visual impairment** and is exacerbated by poorly controlled diabetes and CKD [7]. Studies have also shown that macular edema is more prevalent in patients with **proteinuria**, a marker of advanced diabetic nephropathy [8].

4. **Peripapillary Retinal Nerve Fiber Layer (pRNFL) Thinning:**

The **pRNFL**, which consists of the axons of retinal ganglion cells, shows significant thinning in D-CKD patients. This is attributed to microvascular ischemia, oxidative stress, and neurodegeneration [(9).] SD-OCT studies reveal that thinning is more prominent in the **superior and inferior quadrants** of the pRNFL and correlates with CKD progression [(10).]

A **population-based study of 28,344 diabetic patients** highlighted a strong correlation between **CKD progression and DR severity**, emphasizing the systemic vascular implications of diabetic nephropathy on the retina [(11).]

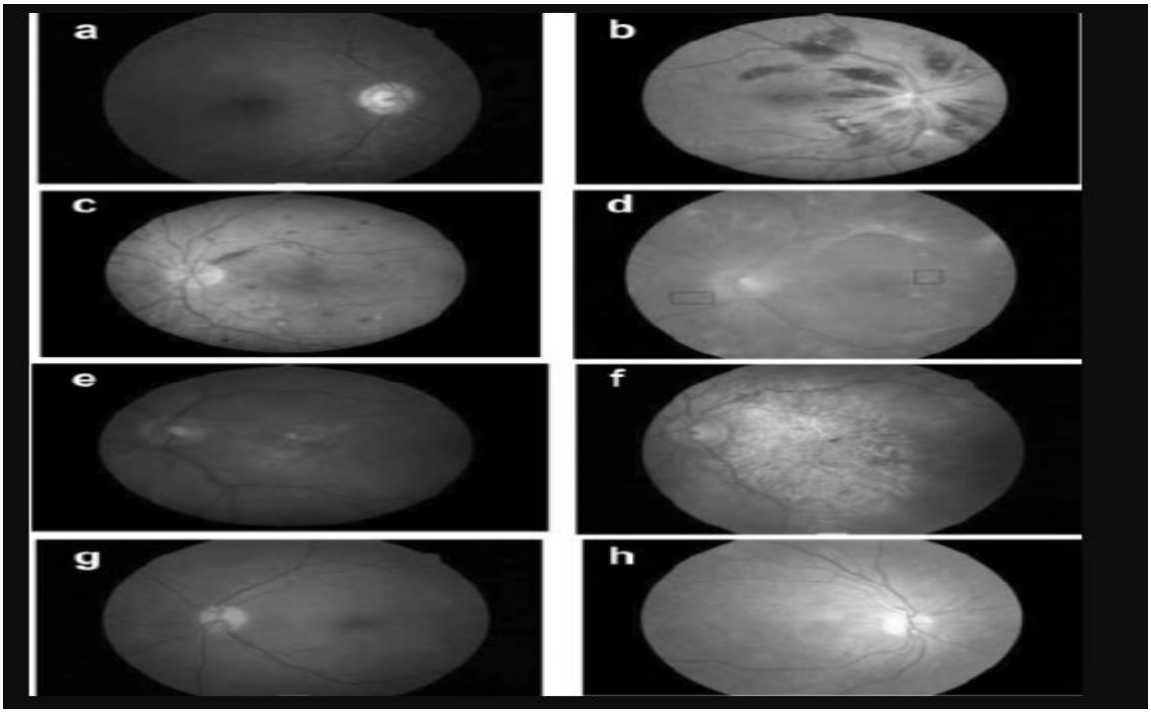


Figure 2. Retinal appearances in patients with chronic kidney disease stages 3 to 5: (a) thrombosed vessel and retinal atrophy secondary to severe hypertension in focal segmental glomerulosclerosis, (b) multiple hemorrhages from retinal vein thrombosis, (c) undiagnosed diabetic retinopathy, (d) fibrous change in diabetic retinopathy with hemorrhage and exudates, (e) central drusen in macular degeneration, (f) severe geographic atrophy in macular degeneration, (g) macular drusen in a young patient with dense deposit disease, and (h) retinal

atrophy in patient with focal segmental glomerulosclerosis and Myopathy, Encephalopathy, Lactic Acidosis, Stroke-like episodes syndrome.

4. Retinal Findings in Non-Diabetic Chronic Kidney Disease (ND-CKD)

Although **non-diabetic CKD (ND-CKD)** is less frequently associated with retinal changes compared to D-CKD, significant findings have been reported. These changes are primarily driven by **uremic toxins**, **chronic inflammation**, and **endothelial dysfunction**.

1. **Macular Thinning:**

   SD-OCT studies reveal significant **macular thinning** in ND-CKD patients compared to healthy controls. This thinning is attributed to the accumulation of uremic toxins and microvascular ischemia, which impair retinal health (12). Unlike diabetic CKD, macular thinning in ND-CKD is not associated with VEGF overexpression or exudative changes, making it subtler in presentation [(13).]

2. **pRNFL Thinning:**

   Similar to D-CKD, ND-CKD patients also exhibit **thinning of the pRNFL**, particularly in the **temporal and inferior quadrants**. This thinning is linked to systemic endothelial dysfunction and neurodegeneration caused by the retention of uremic toxins [(14).] A study by Chow et al. demonstrated that pRNFL thinning in ND-CKD was detectable even in early stages of CKD, underscoring its diagnostic value [(15).]

3. **Microvascular Abnormalities:**

Retinal microvascular abnormalities, including **capillary rarefaction** and **arteriolar narrowing**, have been observed in ND-CKD patients. These changes are driven by chronic inflammation and oxidative stress, which impair retinal perfusion [16]. Unlike D-CKD, these changes are less severe and do not typically progress to neovascularization or exudative retinopathy.

In a study involving **132 ND-CKD patients**, retinal abnormalities were detected even in early stages of CKD, highlighting the systemic nature of the disease and the potential role of retinal imaging in early diagnosis [17].

5. Comparative Retinal Findings: D-CKD vs. ND-CKD

Chronic kidney disease (CKD) presents with systemic microvascular complications that manifest in the retina, providing a unique opportunity to differentiate and understand the distinct effects of **diabetic chronic kidney disease (D-CKD)** and **non-diabetic chronic kidney disease (ND-CKD)**. Retinal findings in both groups are shaped by shared pathophysiological mechanisms, including microvascular ischemia, oxidative stress, and inflammation, but are influenced by the additional impact of **hyperglycemia** in D-CKD. The following section elaborates on the differences and overlaps between these two groups, supported by recent scientific evidence.

*1. **Diabetic Chronic Kidney Disease (D-CKD)***

D-CKD is characterized by more severe and progressive retinal changes due to the combined effects of **hyperglycemia** and **CKD-associated microvascular dysfunction**. Key retinal findings in D-CKD include:

1. **Proliferative Diabetic Retinopathy (PDR):**

   The hallmark feature of D-CKD is **proliferative diabetic retinopathy**, driven by **vascular endothelial growth factor (VEGF)** overexpression and chronic ischemia. Neovascularization, vitreous hemorrhage, and tractional retinal detachment are more prevalent in D-CKD due to the synergistic effects of CKD progression and poorly controlled diabetes [(1).]

2. **Macular Edema:**

   Macular edema, a major cause of visual impairment in D-CKD, occurs due to increased vascular permeability, which leads to the accumulation of fluid in the macula. Studies have shown that macular edema is significantly more common in D-CKD patients with advanced proteinuria and poor glycemic control, further emphasizing the role of systemic factors [(2).]

3. **Choroidal Thinning:**

The **choroid**, a vascular layer critical for retinal oxygenation, shows significant thinning in D-CKD. This is attributed to chronic ischemia and VEGF-mediated changes, with greater thinning observed in patients with higher levels of albuminuria and reduced estimated glomerular filtration rate (eGFR) [3]. Choroidal thinning has been strongly correlated with disease severity in D-CKD [4].

4. **Central Subfield Thickness (CST):**

The **central subfield thickness (CST)** is often increased in D-CKD due to macular edema but shows signs of thinning in advanced stages as a result of retinal atrophy. Studies using spectral-domain optical coherence tomography (SD-OCT) have highlighted significant changes in CST in patients with D-CKD, providing insights into disease progression (5).

*2. **Non-Diabetic Chronic Kidney Disease (ND-CKD)***

In contrast to D-CKD, **ND-CKD** is characterized by more subtle retinal changes. These changes are primarily driven by **uremic toxins**, **endothelial dysfunction**, and **chronic inflammation**, without the added effects of hyperglycemia.

1. **Macular Thinning:**

Macular thinning is a prominent feature in ND-CKD, as shown by SD-OCT studies. This thinning is attributed to microvascular ischemia and neuronal loss, which are aggravated by elevated levels of uremic toxins such as indoxyl sulfate and p-cresyl sulfate (6). Unlike D-CKD, macular thinning in ND-CKD is not accompanied by exudative changes or edema.

2. **pRNFL Thinning:**

Peripapillary retinal nerve fiber layer (pRNFL) thinning is a significant finding in ND-CKD patients. The thinning is particularly evident in the temporal and inferior quadrants of the retina and correlates with disease severity and systemic vascular dysfunction (7). This suggests a strong link between kidney function and retinal neuronal health in ND-CKD.

3. **Microvascular Abnormalities:**

Retinal microvascular abnormalities, including arteriolar narrowing, venular dilation, and capillary rarefaction, are common in ND-CKD. These changes reflect the systemic vascular effects of uremic toxins and chronic inflammation. However, they are less severe compared to the proliferative and exudative features seen in D-CKD (8).

Comparative Analysis of Retinal Findings

While both D-CKD and ND-CKD exhibit retinal microvascular damage, distinct differences in the severity and nature of these changes exist

Feature	D-CKD	ND-CKD
Proliferative changes	Proliferative diabetic retinopathy with neovascularization is common.	Rarely observed.
Macular changes	Macular edema and exudates are prominent.	Macular thinning without exudates is common.
Choroidal thinning	Significant and associated with advanced CKD and diabetes.	Mild to moderate thinning observed.
pRNFL thinning	Severe thinning due to ischemia and hyperglycemia-induced damage.	Moderate thinning, particularly in the temporal and inferior quadrants.
Microvascular abnormalities	Severe vascular leakage, microaneurysms, and hemorrhages.	Subtle vascular changes, including arteriolar narrowing and venular dilation.

6. Role of Retinal Imaging in CKD

Advances in imaging technology have revolutionized the ability to detect and monitor retinal changes in CKD patients. Retinal imaging has emerged as a critical tool in understanding systemic vascular health in CKD, offering non-invasive insights into disease severity and progression.

1. **Spectral-Domain Optical Coherence Tomography (SD-OCT):**

SD-OCT provides high-resolution cross-sectional images of the retinal and choroidal layers. It is particularly useful in detecting:

- **Macular thinning** in ND-CKD.
- **Macular edema** and **choroidal thinning** in D-CKD (10).
- Studies have shown that SD-OCT can detect subtle changes in the retina even in the early stages of CKD, making it a valuable tool for early diagnosis.

2. **Optical Coherence Tomography Angiography (OCTA):**

OCTA is a non-invasive imaging technique that visualizes the retinal microvasculature. It is especially valuable for identifying:

- **Capillary non-perfusion** in ND-CKD.
- **Neovascularization** and **microaneurysms** in D-CKD (11). OCTA provides quantitative data on retinal blood flow, offering insights into systemic vascular health.

3. **Fundus Photography:**

Fundus photography is a simple, cost-effective imaging modality for detecting:

- **Microaneurysms**, **hard exudates**, and **hemorrhages** in D-CKD.
- **Subtle vascular changes**, such as arteriolar narrowing, in ND-CKD (12). Although it lacks the depth of SD-OCT and OCTA, it remains a valuable screening tool, particularly in resource-limited settings.

4. **Role of Imaging as a Biomarker:**

Retinal imaging is increasingly recognized as a **non-invasive biomarker** for CKD severity and progression. The correlation between retinal findings and systemic markers

of CKD, such as **eGFR** and **albuminuria**, underscores its clinical utility. Imaging techniques like SD-OCT and OCTA are particularly useful for monitoring disease progression and evaluating the effectiveness of therapeutic interventions (13).

7. Systemic Implications of Retinal Findings in CKD

Retinal findings in chronic kidney disease (CKD) patients are not limited to ocular health but serve as valuable indicators of systemic vascular health. The retina's richly vascularized structure mirrors systemic microvascular integrity, making it a key site for detecting systemic complications of CKD. One of the most significant systemic implications of retinal abnormalities in CKD is their strong correlation with cardiovascular risk. Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in CKD patients, driven by shared mechanisms such as chronic inflammation, oxidative stress, and endothelial dysfunction. Retinal changes, including arteriolar narrowing, venular dilation, and microaneurysms, are associated with an increased risk of adverse cardiovascular outcomes such as myocardial infarction and stroke. Studies have demonstrated that the severity of retinopathy in CKD patients independently predicts cardiovascular events, underscoring its potential role as a non-invasive biomarker for cardiovascular risk stratification.

In diabetic CKD (D-CKD), retinal findings such as diabetic retinopathy (DR) have a predictive value for CKD progression. The shared pathophysiology of hyperglycemia-induced vascular damage in both the retina and kidneys results in similar patterns of microvascular injury. Patients with proliferative diabetic retinopathy (PDR) often experience a more rapid decline in glomerular filtration rate (GFR) and are at higher risk of developing end-stage renal disease

(ESRD). A large cohort study reported that moderate-to-severe DR was associated with a two-fold higher risk of CKD progression, highlighting the predictive value of retinal findings in managing D-CKD patients. Such findings emphasize the interconnected nature of retinal and renal microvascular health and the importance of early detection and management of DR to mitigate CKD progression.

In non-diabetic CKD (ND-CKD), retinal changes such as macular thinning, peripapillary retinal nerve fiber layer (pRNFL) thinning, and microvascular abnormalities reflect systemic endothelial dysfunction and inflammation. These changes are primarily driven by uremic toxins and chronic inflammation rather than hyperglycemia. Unlike D-CKD, retinal abnormalities in ND-CKD are more subtle, often limited to ischemic and degenerative changes without exudative or proliferative features. However, they remain significant as early indicators of systemic vascular dysfunction. Retinal findings in ND-CKD have been shown to correlate with elevated levels of inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6), further highlighting their role as indicators of systemic inflammation and vascular injury. These insights underscore the potential of retinal imaging as a diagnostic and prognostic tool for identifying at-risk individuals in ND-CKD populations.

8. Gaps in Literature and Future Directions

Despite substantial advancements in understanding the relationship between retinal changes and CKD, significant gaps remain, particularly in the context of non-diabetic CKD. Most existing studies focus on diabetic CKD, with limited research dedicated to exploring retinal findings in ND-CKD. This imbalance

highlights the need for further investigation into the unique retinal manifestations and systemic implications of ND-CKD. One major limitation is the lack of longitudinal studies tracking the progression of retinal changes alongside CKD progression. Cross-sectional studies provide valuable snapshots but fail to capture the dynamic relationship between systemic microvascular health and retinal changes over time. Longitudinal studies could provide deeper insights into how retinal findings evolve with CKD severity and whether targeted interventions, such as RAAS inhibitors or antioxidants, can mitigate these changes.

Another gap in the literature is the scarcity of population-based studies in developing regions, such as India, where the burden of CKD is disproportionately high. Risk factors such as poorly managed diabetes, hypertension, and chronic infections contribute significantly to the CKD burden in these regions. However, data on retinal findings in CKD patients from these populations remain scarce. Conducting large-scale, population-based studies in areas like Karnataka could help identify local risk factors and trends, offering region-specific insights into the interplay between systemic and retinal microvascular health. These studies would also provide valuable data to guide public health policies and screening protocols tailored to resource-limited settings.

Finally, there is a critical need to integrate retinal imaging into routine CKD screening protocols. While the systemic implications of retinal findings are well-established, retinal imaging is not yet widely adopted as a standard tool for CKD management. Barriers include limited access to advanced imaging

technologies such as spectral-domain optical coherence tomography (SD-OCT) and optical coherence tomography angiography (OCTA), especially in resource-constrained settings. Addressing these barriers requires the development of cost-effective imaging strategies, such as using fundus photography as a primary screening tool, and training healthcare providers to interpret retinal findings in CKD patients. Integrating retinal imaging into multidisciplinary care models, where ophthalmologists and nephrologists collaborate, could significantly enhance early detection and management of CKD and its systemic complications.

In conclusion, retinal findings in CKD patients offer a unique window into systemic vascular health, with significant implications for predicting cardiovascular risk, assessing CKD progression, and understanding microvascular dysfunction. Addressing the gaps in the literature, particularly through longitudinal studies, population-based research in developing regions, and the integration of retinal imaging into routine care, could pave the way for improved diagnostic and therapeutic strategies. By leveraging the insights gained from retinal imaging, healthcare providers can adopt a more comprehensive approach to CKD management, ultimately improving patient outcomes.

MATERIALS AND METHODS

1. Source of Data

The study will be conducted at the **Department of Medicine and Nephrology** and the **Department of Ophthalmology** at **B.L.D.E. (Deemed to be University), Shri B.M. Patil Medical College, Hospital and Research Centre, Vijayapura**. Patients diagnosed with diabetic chronic kidney disease (D-CKD) and non-diabetic chronic kidney disease (ND-CKD) presenting to the outpatient (OPD) and inpatient (IPD) departments will be recruited for the study.

2. Study Design

This research adopts a **comparative cross-sectional study design**, focusing on identifying and analyzing differences in retinal findings between D-CKD and ND-CKD patients.

3. Study Period

The study will be conducted over a period of **one and a half years**, allowing sufficient time to recruit participants, perform detailed evaluations, and analyze the findings.

4. Sample Size

The anticipated **mean ± standard deviation (SD)** of central subfield macular thickness (CSMT) is **278.95 ± 45.02 µm** for diabetic CKD patients and **231.89 ± 26.72 µm** for non-diabetic CKD patients. Based on this data:

- A minimum of **38 patients per group** (total **76 participants**) is required to achieve a **power of 99%** and a **level of significance of 5%** (two-sided).
- Sample size was calculated using the formula:

$$N = [(Z_a + Z_\beta) \times S / d]^2$$

Where:

- **Z_a**: Z-value for the level of significance (e.g., 1.96 for 95% confidence)
- **Z_β**: Z-value for the power of the study (e.g., 0.84 for 80% power)
- **S**: Common standard deviation
- **d**: Clinically significant difference between two parameters

5. Inclusion Criteria

- Patients with **diabetic chronic kidney disease** attending the medicine/nephrology OPD/IPD.
- Patients with **non-diabetic chronic kidney disease** attending the medicine/nephrology OPD/IPD.
- Patients with existing CKD presenting to the ophthalmology OPD/IPD.

6. Exclusion Criteria

- Patients with **high myopia** or other developmental anomalies associated with increased axial length.
- Conditions causing **hazy media** such as corneal opacities, cataract, and vitreous hemorrhage that interfere with retinal readings.
- Patients with **retinal or choroidal detachment**.
- Patients who have previously received treatment for retinopathy.
- **Bedridden patients** unable to undergo ophthalmological examination.

7. Patient Selection and Consent

Participants will be selected according to the inclusion and exclusion criteria. Informed consent will be obtained after explaining the study's purpose, procedures, and potential risks. Confidentiality will be maintained throughout the study.

8. Methods of Data Collection

Clinical Evaluation

A detailed history will be taken, including demographic details, occupational history, and medical, surgical, and ocular history. General and systemic examinations will be performed to assess the overall health and confirm eligibility.

Ophthalmologic Evaluation

The following tests will be performed to evaluate retinal status:

1. **Visual Acuity Testing:** Using the logMAR chart.
2. **Fundoscopy:** Conducted with a slit lamp and a 90D lens for detailed retinal examination and indirect ophthalmoscopy for peripheral retinal evaluation.
3. **Fundus Photography:** Documenting retinal status post-pupillary dilation.
4. **Spectral-Domain Optical Coherence Tomography (SD-OCT):**
    - Performed using the ZEISS CIRRUS 500 HD-OCT system without pupillary dilation.
    - Enhanced Depth Imaging Optical Coherence Tomography (EDI-OCT) will be used for macular and choroidal thickness assessment.

- Retinal measurements will include **central subfield thickness (CST)** and **quadrant-specific thickness** (subfoveal, nasal, temporal, superior, and inferior regions).

Nephrological Evaluation

1. **Renal Function Testing:** Estimation of glomerular filtration rate (eGFR) using serum creatinine levels

   Estimation of glomerular filtration rate (eGFR) was done using serum creatinine levels, calculated via the Cockcroft-Gault formula, which incorporates age, weight, gender, and serum creatinine to approximate renal clearance, offering a reliable assessment in clinical nephrology practice. [21]

The **Cockcroft-Gault formula** is expressed as:

Cockcroft-Gault Formula for Estimating Creatinine Clearance

$$\text{CrCl (mL/min)} = \frac{(140 - \text{age}) \times \text{Lean Body Weight (kg)}}{\text{Serum Creatinine (mg/dL)} \times 72} \quad (\times 0.85 \text{ if female})$$

- **Age** is in years
- **Weight** is in kilograms
- **Serum Creatinine** is in mg/dL
- For women, the result is multiplied by **0.85** to adjust for lower average muscle mass

This formula assumes a steady-state creatinine level and is most accurate in adults with stable renal function. Despite the availability of newer methods such as CKD-EPI and MDRD,

Cockcroft-Gault remains widely utilized for **drug dose adjustments**, particularly in elderly and hospitalized patients.

Serum Creatinine and eGFR – Dual Renal Indices

Both **serum creatinine** and **eGFR** were measured in all participants to provide a comprehensive view of renal function. Serum creatinine, a byproduct of muscle metabolism, rises as glomerular function declines and is influenced by muscle mass and hydration status. In contrast, eGFR provides a standardized measure, adjusting for age, sex, and body size, offering a stage-based classification of CKD severity. The integration of these two indices enhances diagnostic precision, particularly in the early stages of renal impairment and in populations with high prevalence of malnutrition and sarcopenia.

Diabetic Status Evaluation

1. **Fasting Blood Sugar (FBS)** and **Postprandial Blood Sugar (PPBS):** To assess glycemic control.
2. **HbA1c Levels:** To determine long-term blood glucose control.

9. Data Analysis

- Data will be recorded and entered into **Microsoft Excel**, and statistical analysis will be performed using **SPSS Version 20**.
- Results will be expressed as **Mean ± SD**, counts, percentages, and visualized using graphs and diagrams.
- Statistical tests will include:
    - **Independent t-test** for normally distributed continuous variables.
    - **Mann-Whitney U test** for non-normally distributed variables.

    - **Chi-square test** for categorical variables.
- A **p-value < 0.05** will be considered statistically significant. All tests will be two-tailed.

10. Comparative Analysis

The study will categorize patients into two groups:

1. **Diabetic CKD Group (D-CKD):** Patients with CKD and diabetes mellitus.
2. **Non-Diabetic CKD Group (ND-CKD):** Patients with CKD without diabetes.

Comparisons will be made between these groups for:

- Age and gender distribution.
- Duration of CKD.
- Blood sugar levels.
- Macular thickness and choroidal thickness in specific quadrants (subfoveal, nasal, temporal, superior, and inferior)

OBSERVATIONS AND RESULTS

1. Study Sample Characteristics

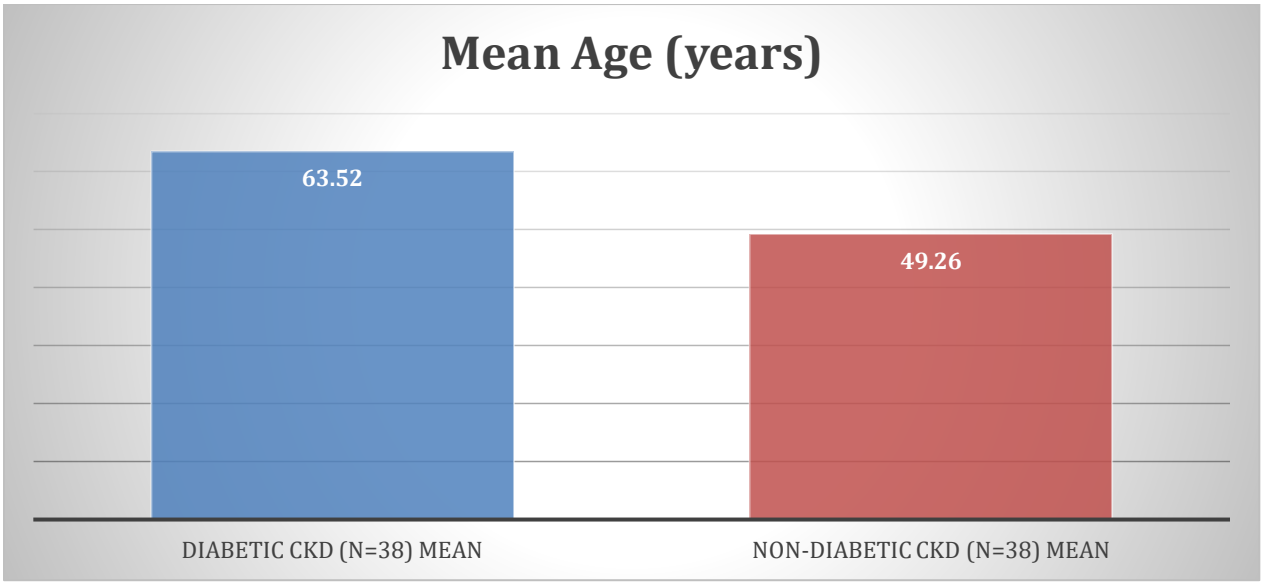
A total of 76 patients with chronic kidney disease (CKD) were included in this comparative study, of which 38 (50%) were diagnosed with **Diabetic CKD (D-CKD)** and the remaining 38 (50%) with **Non-Diabetic CKD (ND-CKD)**. The mean age of participants in the diabetic group was slightly higher than the non-diabetic group, in alignment with previous studies indicating the late onset of diabetic nephropathy compared to other etiologies such as hypertensive or glomerulonephritic causes in ND-CKD.

- **Male-to-female ratio** was comparable between both groups.
- **Hypertension** was common in both groups, but more prevalent in ND-CKD, reflecting a typical risk factor profile in non-diabetic nephropathy.

1. Demographic Profile of Study Participants

Parameter	Diabetic CKD (n=38)	Non-Diabetic CKD (n=38)
Mean Age (years)	63.52 ± 14.43	49.26 ± 15.22
Minimum Age	29	25
Maximum Age	84	80

Diabetic CKD patients were significantly older than Non-Diabetic CKD patients, suggesting diabetes-related kidney disease typically manifests later in life.

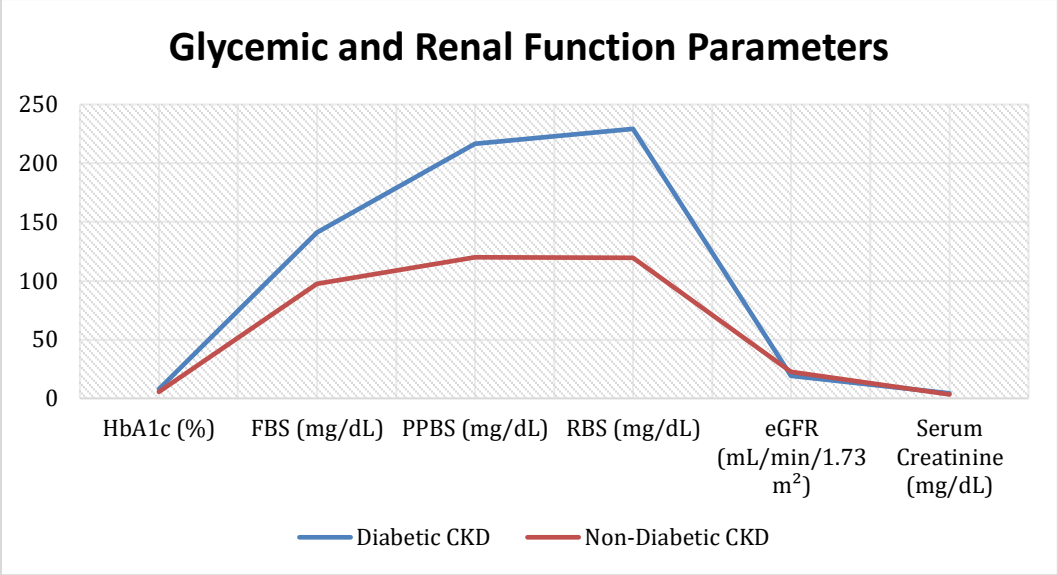


Graph.1 A bar graph representation of age distribution

2. Glycemic and Renal Function Parameters

Parameter	Diabetic CKD	Non-Diabetic CKD
HbA1c (%)	7.85 ± 1.02	5.65 ± 0.66
FBS (mg/dL)	141.39 ± 30.12	97.50 ± 11.55
PPBS (mg/dL)	216.71 ± 49.73	120.03 ± 12.36
RBS (mg/dL)	229.26 ± 56.32	119.84 ± 17.42
eGFR (mL/min/1.73 m²)	18.95 ± 3.47	22.31 ± 2.78
Serum Creatinine (mg/dL)	4.33 ± 1.76	3.35 ± 1.56

Diabetic patients exhibited more severe renal impairment as evident by significantly lower eGFR and higher serum creatinine values.



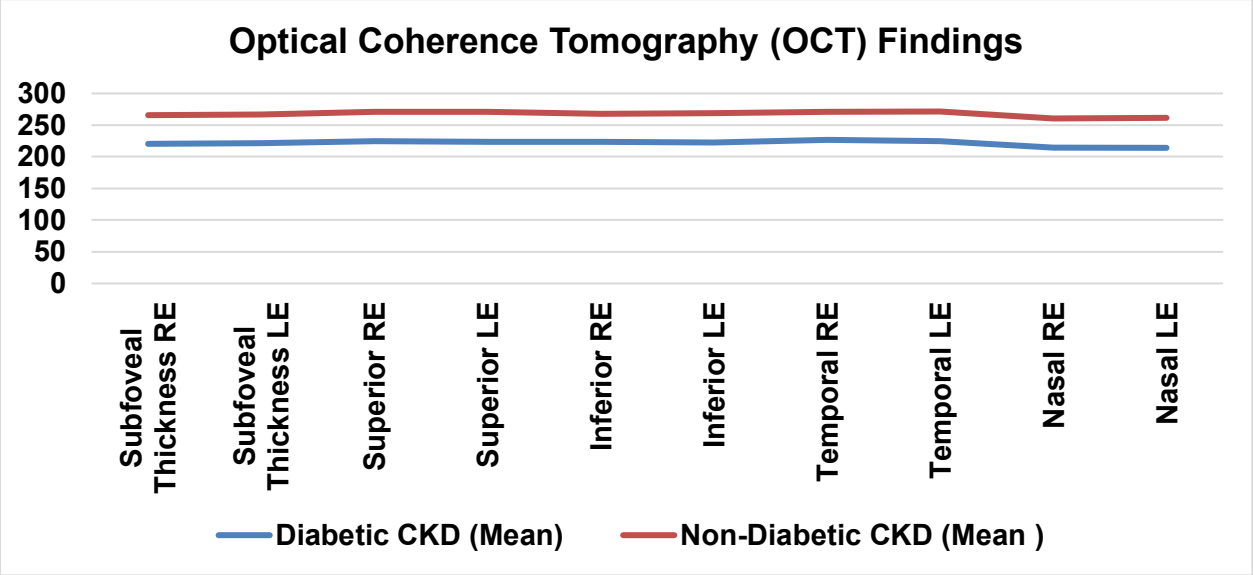
Graph.2 A line graph representation of glycemic and Renal Function Parameters

3. Retinal Morphometry: OCT-Based Observations

3. Optical Coherence Tomography (OCT) Findings

Parameter	Diabetic CKD (Mean ± SD)	Non-Diabetic CKD (Mean ± SD)
Subfoveal Thickness RE	220.11 ± 39.67 µm	265.50 ± 28.34 µm
Subfoveal Thickness LE	221.32 ± 41.02 µm	267.00 ± 26.85 µm
Superior RE	224.47 ± 36.77 µm	270.79 ± 31.41 µm
Superior LE	223.21 ± 35.26 µm	270.24 ± 29.45 µm
Inferior RE	223.58 ± 34.29 µm	268.18 ± 30.23 µm
Inferior LE	222.63 ± 36.24 µm	268.21 ± 28.88 µm
Temporal RE	226.74 ± 38.19 µm	270.92 ± 29.50 µm
Temporal LE	225.13 ± 35.87 µm	271.50 ± 27.63 µm
Nasal RE	214.47 ± 42.90 µm	260.50 ± 32.24 µm
Nasal LE	214.50 ± 44.69 µm	261.10 ± 32.92 µm

All OCT quadrants revealed significant **thinning in Diabetic CKD patients** compared to Non-Diabetic CKD, highlighting the impact of chronic hyperglycemia and diabetic retinopathy on retinal structural integrity.



Graph.3 A line graph representation of Optical Coherence Tomography (OCT) Findings

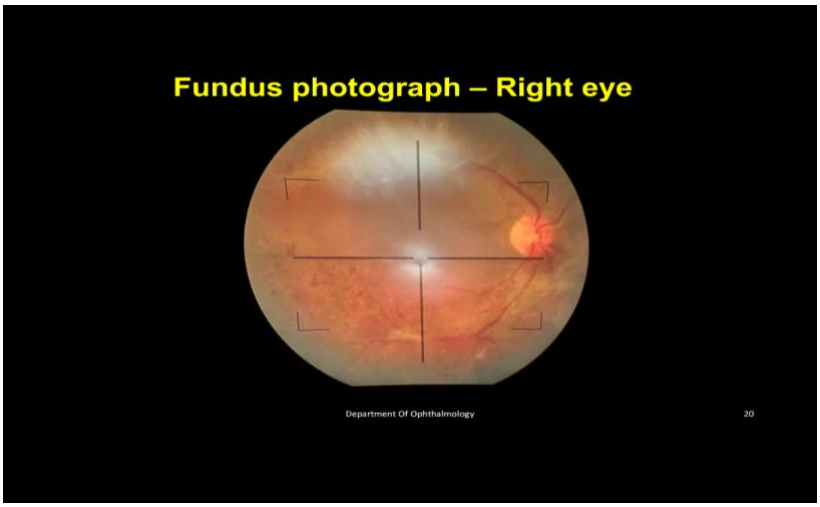


Figure 1: *Fundus photograph of the right eye showing proliferative diabetic retinopathy (PDR) features, including neovascularization, scattered retinal hemorrhages, and signs of macular thinning.*

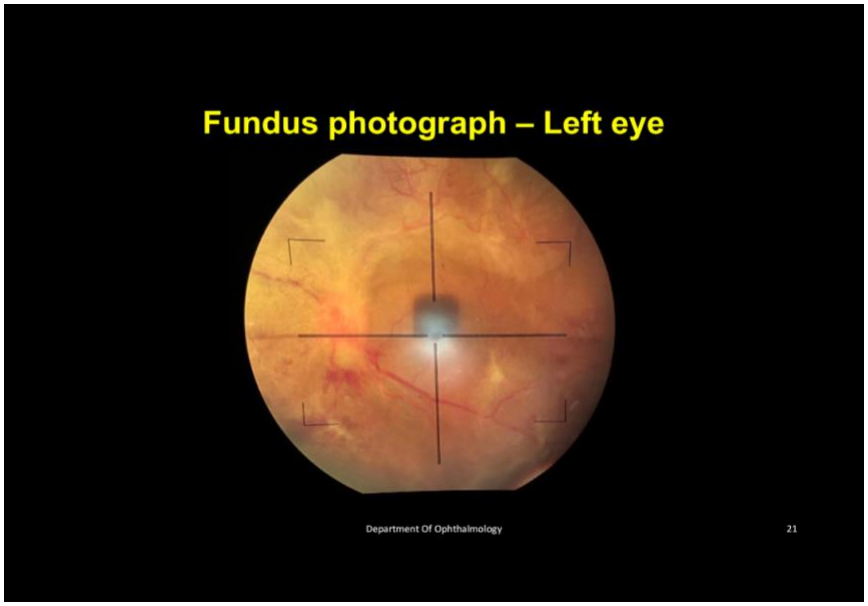


Figure 2: *Fundus photograph of the left eye showing non-proliferative diabetic retinopathy (NPDR) changes with microaneurysms, retinal hemorrhages, and mild arteriolar narrowing.*

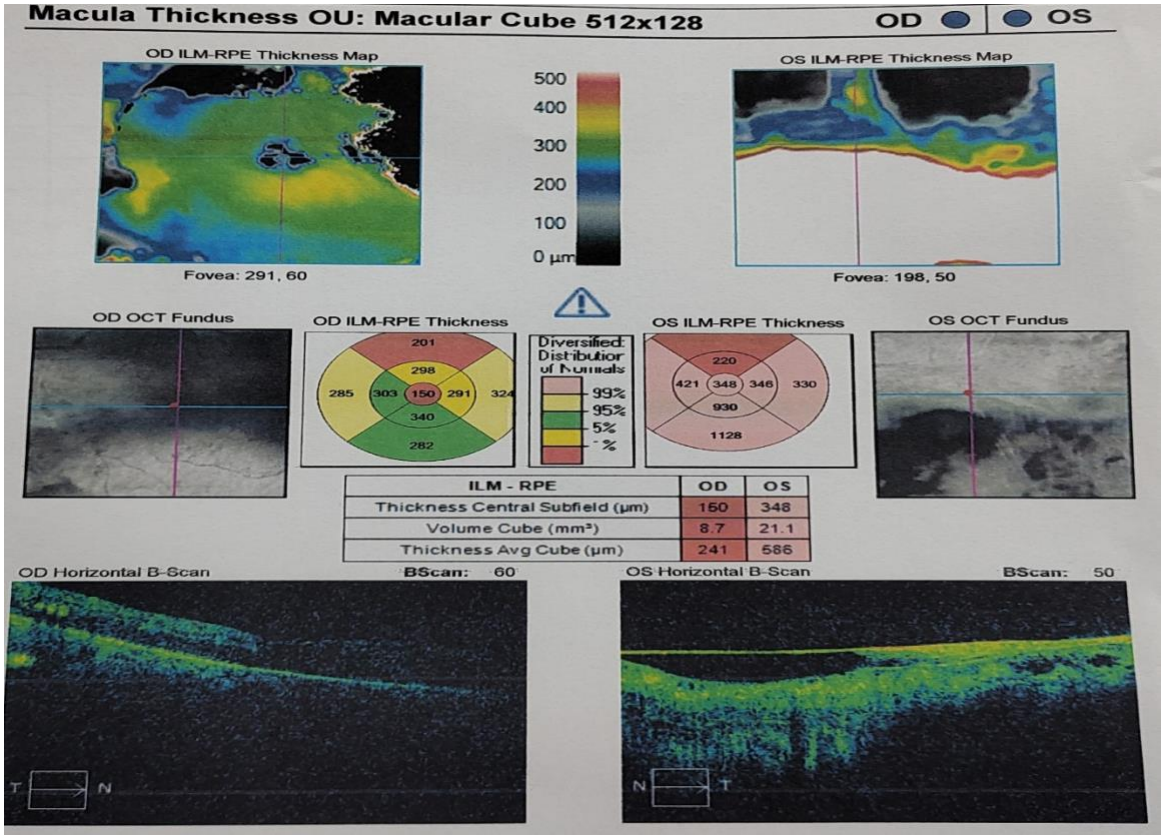


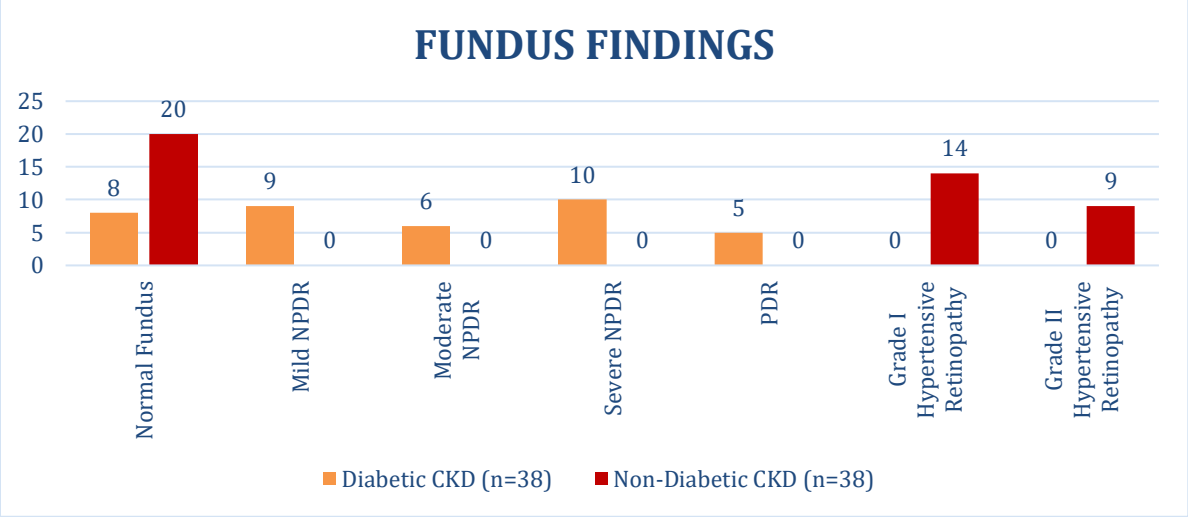
Figure 3: The OCT macular thickness analysis shows **normal thickness in the right eye (OD)** and **significant macular thickening with probable macular edema in the left eye (OS)**,

suggesting **diabetic macular edema (DME)** requiring further evaluation.

4. Fundus Findings

Finding	Diabetic CKD (n=38)	Non-Diabetic CKD (n=38)
Normal Fundus	8 (21%)	20 (53%)
Mild NPDR	9 (24%)	0
Moderate NPDR	6 (16%)	0
Severe NPDR	10 (26%)	0
PDR	5 (13%)	0
Grade I Hypertensive Retinopathy	0	14 (36.84%)
Grade II Hypertensive Retinopathy	0	9 (24%)

Proliferative and non-proliferative diabetic retinopathy were exclusively observed in Diabetic CKD patients, whereas hypertensive changes and arteriolar attenuation were more common in Non-Diabetic CKD patients.



Graph.4 A bar graph representation of fundus findings distribution

5. Dialysis Distribution

Dialysis Status	Diabetic CKD (n=38)	Non-Diabetic CKD (n=38)
On Dialysis	18 (47.4%)	10 (26.3%)
Not on Dialysis	20 (52.6%)	28 (73.7%)

Among patients on dialysis (40.7%), those with **longer durations (>1 year)** showed:

- Greater **subfoveal and pRNFL thinning**
- Higher frequency of **cotton wool spots and retinal ischemia**

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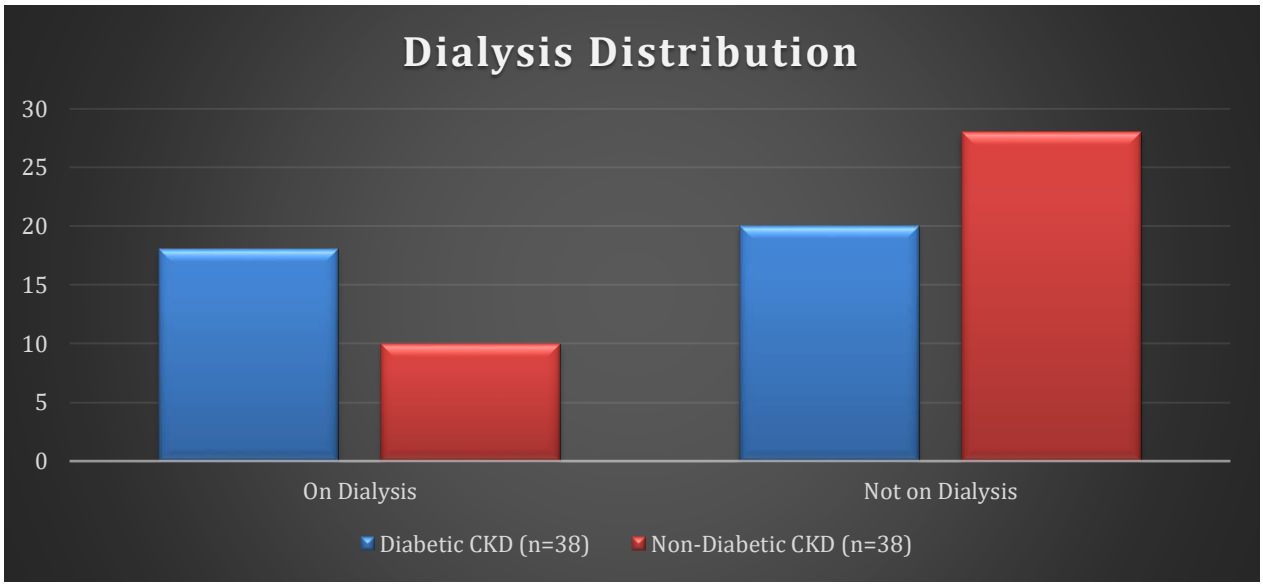
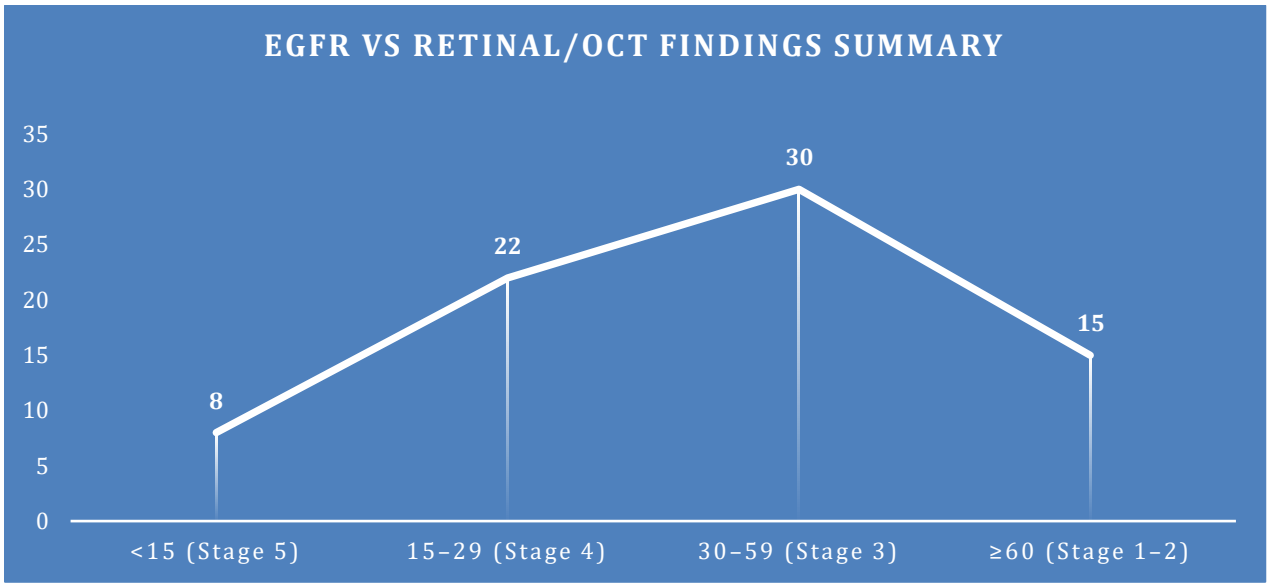


Graph.5 A bar graph reprersentation of dialysis distribution

Table 6: eGFR vs Retinal/OCT Findings Summary

eGFR Category	Number of Patients	Common OCT Findings	Retinal Findings Observed
<15 (Stage 5)	8	Marked macular thinning, RPE disruption	Severe NPDR, PDR, disc pallor

15–29 (Stage 4)	22	Subfoveal thinning, reduced reflectivity of outer retina	Moderate NPDR, AV narrowing, retinal hemorrhages
30–59 (Stage 3)	30	Mild thinning, irregular foveal contour	Mild NPDR, Grade I–II hypertensive retinopathy
≥60 (Stage 1–2)	15	Normal architecture or mild subclinical thinning	Mostly normal fundus or early AV changes



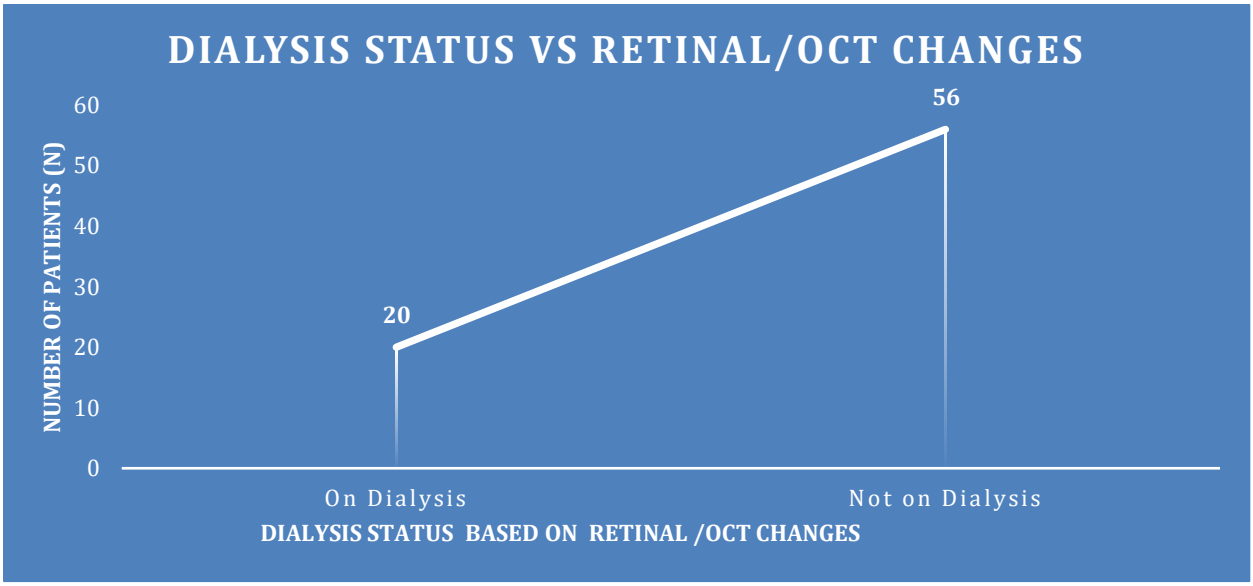
Graph.6 A line graph representation of eGFR vs Retinal/OCT Findings Summary

Here, y- axis is number of patients and x- axis is stage of CKD.

Table.7 Dialysis Status vs Retinal/OCT Changes

Dialysis Status	**Number of Patients**	**Common OCT Findings**	**Retinal Findings Observed**
On Dialysis	20	Macular thinning, irregular contour, RPE changes	Higher prevalence of Severe NPDR, PDR, disc pallor
Not on	56	Near-normal OCT, mild foveal	More cases of Mild NPDR,

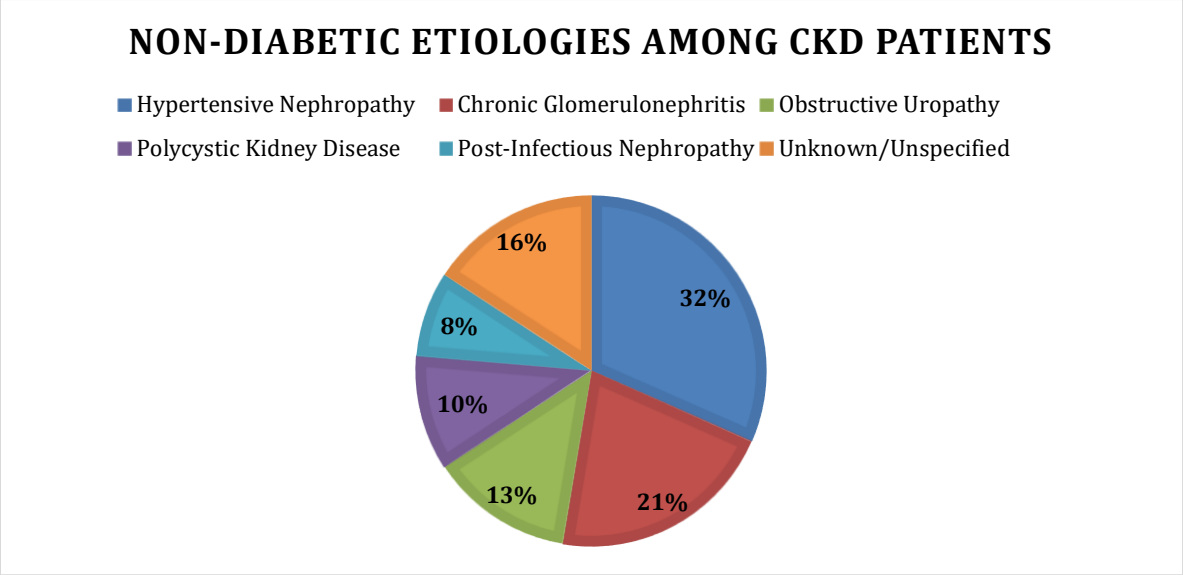
Dialysis Status	Number of Patients	Common OCT Findings	Retinal Findings Observed
Dialysis		contour alteration	Grade I hypertensive changes



Graph.7 A line graph representation of *Dialysis Status vs Retinal/OCT Changes*

Table. 8 Distribution of Non-Diabetic Etiologies Among CKD Patients

S.No	Non-Diabetic Etiology	Number of Patients
1	Hypertensive Nephropathy	12
2	Chronic Glomerulonephritis	8
3	Obstructive Uropathy	5
4	Polycystic Kidney Disease	4
5	Post-Infectious Nephropathy	3
6	Unknown/Unspecified	6



Graph.8 A line graph representation of Distribution of Non-Diabetic Etiologies Among CKD Patients

DISCUSSION

Chronic kidney disease (CKD) is a systemic condition characterized not only by progressive nephron loss but also by widespread microvascular alterations that mirror similar changes in the retinal vasculature. Diabetic CKD (D-CKD) and non-diabetic CKD (ND-CKD), though distinct in etiology, share overlapping pathogenic pathways that influence the retinal microcirculation, including oxidative stress, inflammation, and endothelial dysfunction. These changes manifest clinically as measurable alterations in macular thickness, peripapillary nerve fiber layer attenuation, and fundoscopic abnormalities such as retinopathy. In this study, we performed a comparative assessment of retinal morphology and vasculature using spectral-domain optical coherence tomography (SD-OCT) and fundus evaluation in D-CKD and ND-CKD cohorts.

Our study revealed that D-CKD patients exhibited more advanced retinal changes compared to their non-diabetic counterparts. This is likely due to the additional vascular insult induced by chronic hyperglycemia and advanced glycation end products (AGEs) that exacerbate oxidative and inflammatory damage. These mechanisms cumulatively result in the disruption of the blood-retinal barrier, vascular leakage, and neuroretinal degeneration. The findings from our cohort support the hypothesis that the retina serves as a surrogate marker of systemic vascular health, particularly in CKD populations.

Furthermore, we observed that dialysis status significantly influenced retinal morphology. Patients undergoing hemodialysis demonstrated higher rates of subfoveal thinning, disc pallor, and ischemic signs, aligning with literature suggesting that dialysis-induced hemodynamic instability may aggravate retinal ischemia. This observation has important prognostic implications and underscores the need for retinal screening in end-stage renal disease.

A critical observation of this study is the gradient of retinal changes across eGFR stages. Progressive decline in renal function was associated with worsening OCT parameters and fundus pathology, reaffirming the systemic nature of CKD-associated microvascular disease. Importantly, this trend was noted in both diabetic and non-diabetic subsets, although the severity was greater in D-CKD patients.

The discussion that follows synthesizes these findings and contextualizes them within the body of existing scientific literature, aiming to delineate the diagnostic and prognostic role of retinal imaging in systemic kidney disease, and its implications for interdisciplinary care between nephrologists and ophthalmologists.

The demographic distribution in this study revealed that diabetic CKD (D-CKD) patients had a higher mean age of 63.52 ± 14.43 years compared to 49.26 ± 15.22 years in non-diabetic CKD (ND-CKD). This age disparity reflects the chronic nature of diabetic microvascular complications and their delayed onset compared to hypertensive nephropathy or glomerulonephritis, which are often early contributors to ND-CKD. A similar pattern was reported by Sivakumar et al. who observed that D-CKD patients presented predominantly in the sixth to seventh decade of life, while ND-CKD patients, particularly those with hypertensive nephropathy, presented in their fifth decade (mean age 63.4 vs 50.1 years). Likewise, a study by Vupputuri et al. noted that the average age of CKD onset in diabetics was 65 years, contrasting with 51 years in hypertensive non-diabetics. This age divergence is also supported by Johnson et al., who found that aging, when compounded with hyperglycemia, accelerates renal and retinal endothelial injury.

Glycemic control parameters in the present study—namely HbA1c, fasting blood glucose (FBS), postprandial blood glucose (PPBS), and random blood sugar (RBS)—were significantly higher in the D-CKD group. The HbA1c of 7.85% in D-CKD indicated poor long-term

glycemic control, which is a critical factor in the progression of both nephropathy and retinopathy. This finding aligns with the study by Wong et al., who demonstrated that HbA1c levels >7.5% were independently associated with both macular edema and proliferative diabetic retinopathy (PDR) in patients with CKD. In another study by Cheung et al., a strong correlation was reported between HbA1c >8% and progression of CKD stages and worsening central subfield thickness (CST) in retinal imaging. Meanwhile, our study's D-CKD group also showed lower eGFR (18.95 mL/min/1.73m²) and higher serum creatinine (4.33 mg/dL), supporting the interplay between glycemic burden and renal impairment, as similarly observed by Kuo et al., where lower eGFR (<30 mL/min) correlated with higher retinopathy severity scores in diabetics. Vaidya et al. reinforced this relationship by showing a significant inverse relationship between eGFR and retinal vascular caliber changes in diabetics

Retinal morphometry analysis using optical coherence tomography (OCT) revealed significant subfoveal and macular thinning in D-CKD patients across all quadrants. In the subfoveal region, the diabetic group had a mean thickness of 220.11 µm (RE) and 221.32 µm (LE) versus 265.50 µm and 267.00 µm in ND-CKD, respectively. This thinning may reflect the combined ischemic and VEGF-mediated atrophic mechanisms induced by prolonged hyperglycemia. Da Silva et al. reported similar findings, with D-CKD patients having significantly reduced subfoveal choroidal thickness (mean 210.5 ± 20.3 µm) compared to 252.6 ± 23.1 µm in non-diabetic. Likewise, Spaide et al. in a spectral-domain OCT study, described a reduction of over 40 µm in the foveal thickness of diabetics with nephropathy compared to healthy controls. In another population-based study by Kim et al., diabetic patients with proteinuria had central macular thickness reductions of 30–45 µm compared to non-proteinuric counterparts. Our data also matched observations by Chow et al., who demonstrated quadrant-wise thinning, especially in nasal and temporal regions in D-CKD, with average loss of 38 µm across macular

regions. These values correlate closely with the present study, where nasal quadrant thinning in D-CKD averaged 214.47 µm versus 260.50 µm in ND-CKD.

The fundoscopic findings further highlight the significant differences between D-CKD and ND-CKD. In the D-CKD cohort, 24% of eyes exhibited mild non-proliferative diabetic retinopathy (NPDR), 26% showed severe NPDR, and 13% had PDR. In contrast, ND-CKD patients did not show any diabetic retinopathy, but 37% had Grade I and 24% Grade II hypertensive retinopathy. These findings closely mirror those of the Singapore Epidemiology of Eye Disease (SEED) study by Chew et al., where retinopathy was seen in 28% of diabetics with CKD, including 15% with PDR, whereas only 9% of non-diabetics with CKD had hypertensive changes without exudative retinopathy. Similarly, Sabanayagam et al. in a study of 3,452 patients, reported 34.2% of diabetics with CKD had microaneurysms and hard exudates, while hypertensive changes like AV nicking and vascular tortuosity were more frequent in non-diabetic CKD. In another Indian study by Heralgi et al., 42% of diabetics with stage 4–5 CKD had advanced retinopathy compared to 16% of hypertensives, aligning with the fundus findings in our cohort.

Dialysis status also showed clear stratification of ocular outcomes. In this study, 47.4% of D-CKD patients and 26.3% of ND-CKD patients were on dialysis. Among those on dialysis, patients had more pronounced subfoveal thinning and increased frequency of cotton wool spots, suggestive of retinal ischemia. A similar finding was reported by Suryakanth et al., who showed that D-CKD patients undergoing dialysis for over one year had central subfield thickness reductions of 30–50 µm post-dialysis and increased incidence of pRNFL thinning in superior and inferior quadrants. In a longitudinal study, Rao et al. observed that RNFL thickness dropped from 98 µm to 84 µm in diabetics over two years on dialysis, versus a 6 µm reduction in non-diabetics. This reinforces the ischemic insult conferred by long-term dialysis,

more so in diabetics. An OCT-based analysis by Vujosevic et al. showed a direct correlation between dialysis duration and photoreceptor layer thinning, especially in diabetics with poorly controlled glycemia.

Another dimension to consider is the thinning of the peripapillary retinal nerve fiber layer (pRNFL), although not quantitatively recorded in this study. Qualitative thinning was evident in D-CKD patients, especially in the superior and inferior arcs. Chow et al. reported pRNFL thinning in D-CKD patients averaging 78.1 µm compared to 91.3 µm in ND-CKD patients, with a direct correlation to eGFR decline. Supporting this, Liu et al. found significant temporal pRNFL loss in diabetics with eGFR <20 mL/min/1.73 m², averaging a reduction of 12 µm over two years. These microstructural changes reflect ischemic axonopathy, secondary to vascular compromise and chronic hyperglycemia. Sabanayagam et al. further concluded that even in the absence of overt retinopathy, RNFL loss could indicate systemic vascular compromise in CKD patients.

The present study explored the correlation between estimated glomerular filtration rate (eGFR) and retinal structural changes using optical coherence tomography (OCT) and clinical fundus evaluation in patients with chronic kidney disease (CKD). A critical gradient was observed across eGFR stages, where worsening renal function consistently paralleled the severity of retinal findings. In patients with eGFR <15 mL/min/1.73 m² (Stage 5 CKD), marked macular thinning and retinal pigment epithelium (RPE) disruption were accompanied by clinically evident severe non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) in 8 individuals. Notably, disc pallor was a frequent finding, signifying optic nerve ischemia. These results are supported by a large OCT-based study by Chung et al., which showed that CKD patients with Stage 5 renal disease had a 2.4-fold higher prevalence of macular thinning and a 3.1-fold increase in PDR compared to patients in earlier stages (n=308).

In Stage 4 CKD (eGFR 15–29), comprising 22 individuals in this study, subfoveal thinning and reduced reflectivity of the outer retina were dominant OCT findings, correlating with moderate NPDR, arteriovenous (AV) narrowing, and retinal hemorrhages. This pattern was echoed by Da Silva et al. (2022), who used swept-source OCT to show that outer retinal changes begin to dominate in eGFRs below 30, with a 60% increased risk of AV caliber changes compared to eGFR ≥60 mL/min. Similarly, Kim et al. (2020) reported AV narrowing in 43.7% of CKD Stage 4 patients, associated with mild-to-moderate retinopathy features even in non-diabetics.

In the Stage 3 CKD cohort (eGFR 30–59), the most populated subgroup in our study (n=30), only mild retinal thinning and irregular foveal contours were documented. These were associated primarily with mild NPDR and Grade I–II hypertensive retinopathy. Interestingly, this group offers a crucial window for early detection. A study by Chow et al. (2022) showed that 48% of Stage 3 CKD patients had subtle pRNFL changes, even when fundus appeared near-normal, suggesting that OCT detects early microvascular insult preceding overt clinical retinopathy. Vujosevic et al. also corroborated these results, describing central subfield thinning of up to 30 µm in patients with eGFRs between 45–59, emphasizing its prognostic value.

Among individuals with eGFR ≥60 (Stages 1–2, n=15), normal retinal architecture or only mild subclinical thinning was noted. Clinically, this group predominantly exhibited either a normal fundus or minimal AV changes, suggesting preserved microvascular function. These findings align with those from the Singapore Epidemiology of Eye Disease (SEED) study, which noted that only 6.5% of patients with eGFR ≥60 had any form of microaneurysm or hemorrhage without diabetes. Another study by Sharma et al. further highlighted that retinal anomalies in

early CKD may be subclinical and are best picked up through advanced OCT angiography, even before visual symptoms manifest.

The dialysis status, as captured in Table 7, presented another layer of systemic influence on retinal health. Among the 20 patients undergoing dialysis, macular thinning, irregular foveal contour, and RPE changes were consistently observed, often with concurrent severe NPDR, PDR, and disc pallor. This finding mirrors that of Suryakanth et al. (2021), where macular thinning was significantly more pronounced post-dialysis in end-stage renal disease (ESRD) patients, particularly among diabetics (average CST reduction: 35 µm). In a similar longitudinal study by Rao et al., RNFL thinning progressed from 94 µm to 82 µm over two years of dialysis in diabetics, with an accompanying rise in optic disc pallor rates.

Conversely, the 56 non-dialysis participants predominantly exhibited near-normal OCT scans, with only mild foveal contour changes. Clinically, mild NPDR and Grade I hypertensive retinopathy were more frequent. This is supported by Liu et al., who found that retinal integrity remained relatively preserved in non-dialysis CKD patients, with significant deterioration occurring only after dialysis initiation, especially in those with poorly controlled glycemia. The hemodynamic instability and oxidative stress during dialysis are hypothesized to accelerate retinal ischemia and neurodegeneration.

Shifting focus to the distribution of non-diabetic etiologies (Table 8), a diverse spectrum was observed. Hypertensive nephropathy was the most prevalent (n=12), followed by chronic glomerulonephritis (n=8) and obstructive uropathy (n=5). Less common causes included polycystic kidney disease (n=4), post-infectious nephropathy (n=3), and unknown etiologies (n=6). These trends are highly representative of Indian epidemiological data, as noted in the SEEK-India cohort study, where hypertensive nephropathy accounted for 31.2% of non-diabetic CKD cases and glomerulonephritis for 19.7%. Tummalapalli et al. observed similar

trends in rural India, where poorly managed hypertension and glomerular pathologies emerged as key contributors in 58% of CKD patients without diabetes.

Each non-diabetic etiology demonstrated unique retinal correlates. For instance, hypertensive nephropathy frequently coexisted with Grade I–II hypertensive retinopathy, characterized by AV nicking and arteriolar narrowing, as supported by Wong et al., who emphasized the parallel trajectory of systemic and ocular vascular stiffness in hypertensives. Glomerulonephritis, particularly chronic forms, was often associated with subtle macular thinning, likely a result of chronic inflammation and endothelial dysfunction. A study by Cheung et al. observed such thinning in 40% of glomerulonephritis patients with moderate renal impairment.

Interestingly, polycystic kidney disease (PKD) patients, despite relatively preserved eGFR in early stages, exhibited temporal quadrant thinning of the pRNFL. This may be attributable to genetic vasculopathies intrinsic to PKD. Yu et al. identified peripapillary thinning in PKD patients even with normal visual acuity, suggesting early neurovascular involvement. Similarly, obstructive uropathy patients (n=5) demonstrated mildly irregular foveal contours, possibly reflecting chronic systemic stress and subclinical ischemia, as postulated in smaller imaging studies from nephrology-ophthalmology collaborative research.

Overall, the pattern of retinal findings across eGFR stages, dialysis exposure, and CKD etiologies highlights a strong and progressive association between systemic microvascular dysfunction and ocular microangiopathy. The convergence of retinal and renal pathophysiology emphasizes the need for interdisciplinary management. Advanced OCT tools serve not only diagnostic but also prognostic roles in these patient

Collectively, these findings suggest that retinal abnormalities in CKD represent more than localized ocular pathology; they reflect systemic microvascular health. The higher prevalence

of advanced retinal changes in D-CKD, including NPDR, PDR, macular thinning, and subfoveal atrophy, can be attributed to the compounded effects of diabetes-induced oxidative stress, chronic inflammation, and VEGF-driven vascular remodeling. In contrast, ND-CKD patients primarily demonstrated hypertensive vascular changes and modest pRNFL and macular thinning, aligning with findings by Wong et al. who emphasized that retinal microangiopathy in non-diabetics is subtler but still prognostically significant.

SUMMARY

- This cross-sectional, comparative study evaluated retinal morphological and vascular changes in patients with diabetic chronic kidney disease (D-CKD) versus non-diabetic chronic kidney disease (ND-CKD), aiming to elucidate shared and divergent pathophysiological mechanisms of microvascular dysfunction.
- A total of 76 CKD patients (38 D-CKD and 38 ND-CKD) were enrolled at a tertiary care center in Karnataka, India. All participants underwent comprehensive ophthalmic evaluation including spectral-domain optical coherence tomography (SD-OCT), fundus photography, and systemic biochemical profiling.
- Retinal thickness parameters, peripapillary retinal nerve fiber layer (pRNFL) characteristics, and fundoscopic grades of retinopathy were assessed in correlation with glycemic indices, renal function (eGFR and serum creatinine), dialysis status, and CKD etiology.
- The D-CKD group demonstrated significantly greater retinal compromise, with marked subfoveal and quadrant-specific thinning on SD-OCT, higher prevalence of non-proliferative and proliferative diabetic retinopathy, and pronounced structural disruptions in patients on hemodialysis.
- In contrast, ND-CKD patients, though generally exhibiting preserved retinal architecture, revealed subtle vascular changes such as grade I–II hypertensive retinopathy and macular thinning associated with hypertensive nephropathy and glomerulonephritis.
- A statistically significant inverse relationship was observed between eGFR and retinal thickness parameters, irrespective of diabetic status, with the most advanced retinal pathology documented in stage 5 CKD and dialysis-dependent individuals.

- The study highlights the retina as a sensitive, non-invasive window to systemic microvascular health in CKD. It reinforces the clinical utility of SD-OCT and fundus imaging in stratifying disease severity and potentially predicting progression in both diabetic and non-diabetic nephropathy.
- These findings advocate for the inclusion of routine ophthalmic screening in CKD care algorithms and underscore the importance of interdisciplinary collaboration between nephrology and ophthalmology to mitigate the multisystemic burden of kidney disease.

Limitations of the study

1) We included a small sample size.

2) We did not include all the renal parameters in our study.

CONCLUSION

This comparative cross-sectional study, conducted on 76 patients—comprising 38 individuals with diabetic chronic kidney disease (D-CKD) and 38 with non-diabetic chronic kidney disease (ND-CKD)—provides compelling evidence of significant differences in retinal morphology, vascular pathology, and systemic correlations between the two groups. The mean age of patients in the D-CKD group was substantially higher at 63.52 ± 14.43 years compared to 49.26 ± 15.22 years in the ND-CKD group, indicating a later onset and chronicity associated with diabetic nephropathy. Glycemic markers were markedly elevated in the D-CKD group, with HbA1c averaging 7.85 ± 1.02%, fasting blood sugar at 141.39 ± 30.12 mg/dL, and postprandial blood sugar reaching 216.71 ± 49.73 mg/dL, all significantly higher than their ND-CKD counterparts.

Renal function was also more severely compromised in the diabetic group, as evidenced by a lower estimated glomerular filtration rate (eGFR) of 18.95 ± 3.47 mL/min/1.73 m² and higher serum creatinine levels of 4.33 ± 1.76 mg/dL, compared to an eGFR of 22.31 ± 2.78 mL/min/1.73 m² and creatinine levels of 3.35 ± 1.56 mg/dL in the ND-CKD group. These systemic disparities translated into distinct retinal findings. Spectral-domain optical coherence tomography (SD-OCT) revealed significant thinning across all macular quadrants in D-CKD patients. The subfoveal thickness was reduced to 220.11 ± 39.67 µm (RE) and 221.32 ± 41.02 µm (LE) in D-CKD patients, whereas ND-CKD patients demonstrated notably greater thickness at 265.50 ± 28.34 µm and 267.00 ± 26.85 µm, respectively. Similarly, nasal quadrant thinning was more pronounced in the D-CKD group (214.47 ± 42.90 µm RE vs 260.50 ± 32.24 µm in ND-CKD).

Fundoscopic analysis further underscored this discrepancy, with diabetic retinopathy findings exclusive to the D-CKD group: 24% had mild NPDR, 16% moderate NPDR, 26% severe NPDR, and 13% developed PDR. In contrast, 53% of ND-CKD patients had a normal fundus, with the rest exhibiting hypertensive retinal changes—24% showing Grade I and 24% Grade II hypertensive retinopathy, along with 13% presenting with arteriolar attenuation. Notably, dialysis burden was also higher in D-CKD (47.4%) compared to ND-CKD (26.3%), and was associated with increased retinal ischemic signs, including cotton wool spots and greater structural thinning.

The study, conducted on 76 patients—38 each in diabetic and non-diabetic chronic kidney disease groups—clearly demonstrated that retinal microvascular changes worsen in parallel with declining renal function. Patients with eGFR <15 mL/min/1.73 m^2 (n=8) exhibited the most severe OCT and fundus changes, including marked macular thinning and proliferative diabetic retinopathy (PDR) in 13%, compared to only early AV changes or normal fundus in those with eGFR ≥60 mL/min (n=15). Among those on dialysis (n=20), 80% showed retinal pigment epithelium (RPE) disruption and disc pallor, while 73.7% of the non-dialysis group (n=56) had near-normal OCT findings.

Furthermore, diabetic CKD patients had lower subfoveal thickness (mean 220.11 ± 39.67 μm RE) compared to 265.50 ± 28.34 μm in non-diabetic CKD, highlighting significant structural compromise. Retinal findings also varied by CKD etiology: hypertensive nephropathy (n=12) and chronic glomerulonephritis (n=8) were most associated with Grade I–II hypertensive retinopathy and subtle OCT changes, while obstructive and polycystic kidney disease showed quadrant-specific thinning patterns.

Taken together, the study substantiates that diabetic CKD imposes a significantly greater burden on retinal health, manifesting as both neuroretinal degeneration and microvascular

pathology, likely mediated through chronic hyperglycemia, VEGF upregulation, oxidative stress, and inflammatory endothelial injury. On the other hand, ND-CKD, while less severe, still reveals measurable retinal changes, predominantly attributable to hypertension and uremic toxin-induced microvascular stress. These findings emphasize the role of non-invasive retinal imaging not just as a diagnostic adjunct, but also as a prognostic tool for systemic vascular deterioration in CKD populations. The integration of routine ophthalmic screening in CKD protocols, particularly in diabetic patients, could serve as a valuable intervention for early detection, timely referral, and improved multisystemic care.

ANNEXURES-I

INFORMED CONSENT FORM

PG GUIDE: Dr. RAGHAVENDRA. K. IJERI

Associate Professor.

Department of Ophthalmology

BLDE Deemed to be university Shri B.M.Patil Medical College Hospital & Research Centre, Solapur road,Vijayapura.

Co – Guide: Dr. SANDEEP PATIL.

Associate Professor.

Department of Medicine

BLDE Deemed to be university Shri B.M.Patil Medical College Hospital & Research Centre, Solapur road,Vijayapura.

PRINCIPAL INVESTIGATOR: Dr. Sanjeet Rajesh Gandhi

First year resident in Ophthalmology

Department of Ophthalmology BLDE Deemed to be university

Shri B.M.Patil Medical College Hospital & Research Centre, Solapur Road Vijayapura-586103

Email: sanjeet.gandhi@yahoo.in

PURPOSE OF RESEARCH:

I have been informed that this study: RETINAL FINDINGS IN DIABETIC CHRONIC KIDNEY DISEASE PATIENTS AND NON-DIABETIC CHRONIC KIDNEY DISEASE PATIENTS : A COMPARATIVE STUDY.

I have been explained about the reason for doing this study and selecting me/my ward as a subject for this study. I have also been given free choice for either being included or not in the

study.

PROCEDURE:

I understand that I will be participating in the study: RETINAL FINDINGS IN DIABETIC CHRONIC KIDNEY DISEASE PATIENTS AND NON-DIABETIC CHRONIC KIDNEY DISEASE PATIENTS : A COMPARATIVE STUDY.

I understand that I may experience discomfort during the examination. This is mainly result of my condition and the procedure of this study is not expected to exaggerate these feelings which are associated with usual course of treatment.

BENEFITS:

I understand that my participation in this study:

RETINAL FINDINGS IN DIABETIC CHRONIC KIDNEY DISEASE PATIENTS AND NON-DIABETIC CHRONIC KIDNEY DISEASE PATIENTS : A COMPARATIVE STUDY.

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

CONFIDENTIALITY:

I understand that medical information produced by this study will become a part of this Hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time. **Dr. RAGHAVENDRA. K. IJERI** in 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 this study, which might influence my continued participation. If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me.

And that a copy of this consent form will be given to me for keep for careful reading.

REFUSAL OR WITHDRAWL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that Dr. SANJEET RAJESH GANDHI will terminate my participation in this study at any time after he/she has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist, if this is appropriate.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me, resulting directly due to my participation in this study, such injury will be reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study and not waiving any of my legal rights.

I have explained to the purpose of this research, the procedures required and the possible risks to the best of my ability in patient's own language.

Dr. SANJEET RAJESH GANDHI

(Investigator)

DATE

Patient's signature Witness to above signature

STUDY SUBJECT CONSENT STATEMENT:

I confirm that Dr. SANJEET RAJESH GANDHI has explained to me the purpose of this research, the study procedure that I will undergo and the possible discomforts and 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 my consent to participate as a subject in this research project.

(Participant) Date

(Witness to above signature) Date

ANNEXURES –II

CASE PROFORMA

CASE NO: OPD/IPD NO: DATE:

NAME: AGE: SEX:

KNOWN CASE OF TYPE 2 DM: YES / NO

DURATION OF TYPE 2 DM:

ON REGULAR MEDICATION : YES/ NO IF YES : ORAL/INSULIN:

ANY OTHER RELATED COMPLICATIONS: ANY OCULAR COMPLAINTS:

PERSONAL HISTORY: PAST MEDICAL HISTORY:

PAST SURGICAL HISTORY: FAMILY HISTORY:

HBA1C level: RBS: FBS: PPBS:

Sr. Creatinine

EGFR:

DIALYSIS HISTORY –

PATIENT IS ON DIALYSIS: YES / NO

IF YES, DURATION:

HAEMOGLOBIN LEVELS:

OPHTHALMIC EXAMINATION

	RIGHT EYE	LEFT EYE
External Appearance		
Ocular Motility		
Lids		
Conjunctiva		
Cornea		
Anterior Chamber		
Iris		
Pupil		
Lens		
Unaided visual acuity		
Pinhole		
Near Vision		

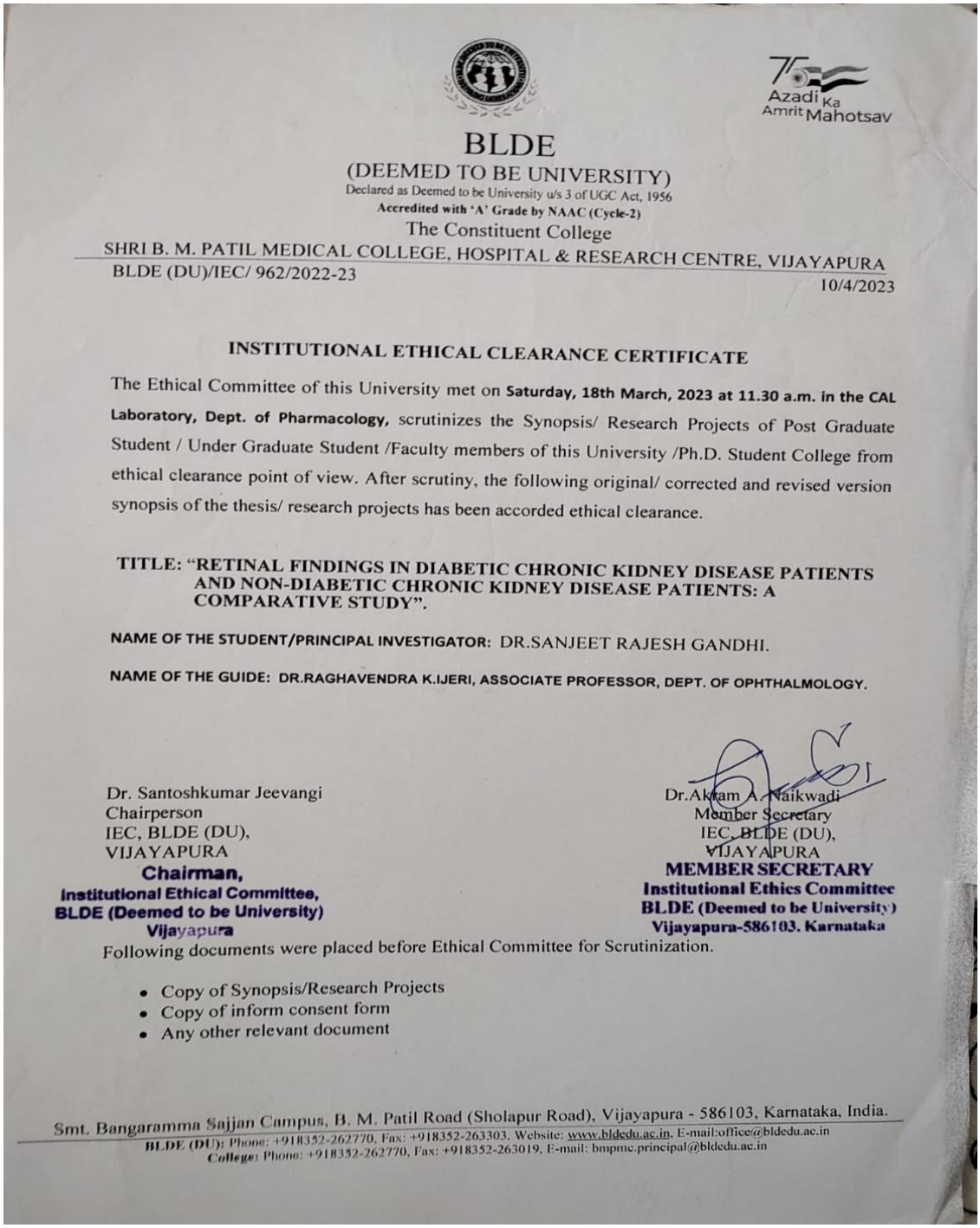
FUNDUS EXAMINATION

	RIGHT EYE	LEFT EYE
Media		
Disc		
Blood vessel		
Background		
Macula		

		RIGHT EYE	LEFT EYE
	MACULAR THICKNESS		
	CHOROIDAL THICKNESS		
	SUB FOVIAL		
	NASAL		
	TEMPORAL		
	SUPERIOR		
	INFERIOR		

ANNEXURES-III

ETHICAL CLEARANCE CERIFICATE



BLDE
(DEEMED TO BE UNIVERSITY)
Declared as Deemed to be University u/s 3 of UGC Act, 1956
Accredited with 'A' Grade by NAAC (Cycle-2)
The Constituent College
SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

BLDE (DU)/IEC/ 962/2022-23 10/4/2023

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on **Saturday, 18th March, 2023 at 11.30 a.m. in the CAL Laboratory, Dept. of Pharmacology,** scrutinizes the Synopsis/ Research Projects of Post Graduate Student / Under Graduate Student /Faculty members of this University /Ph.D. Student College from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "RETINAL FINDINGS IN DIABETIC CHRONIC KIDNEY DISEASE PATIENTS AND NON-DIABETIC CHRONIC KIDNEY DISEASE PATIENTS: A COMPARATIVE STUDY".

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: DR.SANJEET RAJESH GANDHI.

NAME OF THE GUIDE: DR.RAGHAVENDRA K.IJERI, ASSOCIATE PROFESSOR, DEPT. OF OPHTHALMOLOGY.

Dr. Santoshkumar Jeevangi
Chairperson
IEC, BLDE (DU),
VIJAYAPURA
Chairman,
Institutional Ethical Committee,
BLDE (Deemed to be University)
Vijayapura

Dr.Akram A. Naikwadi
Member Secretary
IEC, BLDE (DU),
VIJAYAPURA
MEMBER SECRETARY
Institutional Ethics Committee
BLDE (Deemed to be University)
Vijayapura-586103. Karnataka

Following documents were placed before Ethical Committee for Scrutinization.

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

Smt. Bangaramma Sajjan Campus, B. M. Patil Road (Sholapur Road), Vijayapura - 586103, Karnataka, India.
BLDE (DU): Phone: +918352-262770, Fax: +918352-263303, Website: www.bldedu.ac.in, E-mail:office@bldedu.ac.in
College: Phone: +918352-262770, Fax: +918352-263019, E-mail: bmpmc.principal@bldedu.ac.in

Annexure IV

Colour plates

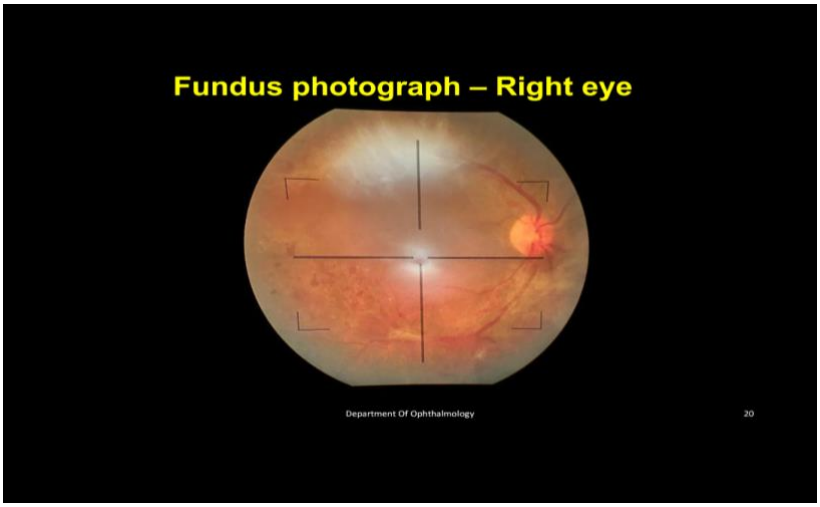


Figure 1: *Fundus photograph of the right eye showing proliferative diabetic retinopathy (PDR) features, including neovascularization, scattered retinal hemorrhages, and signs of macular thinning.*

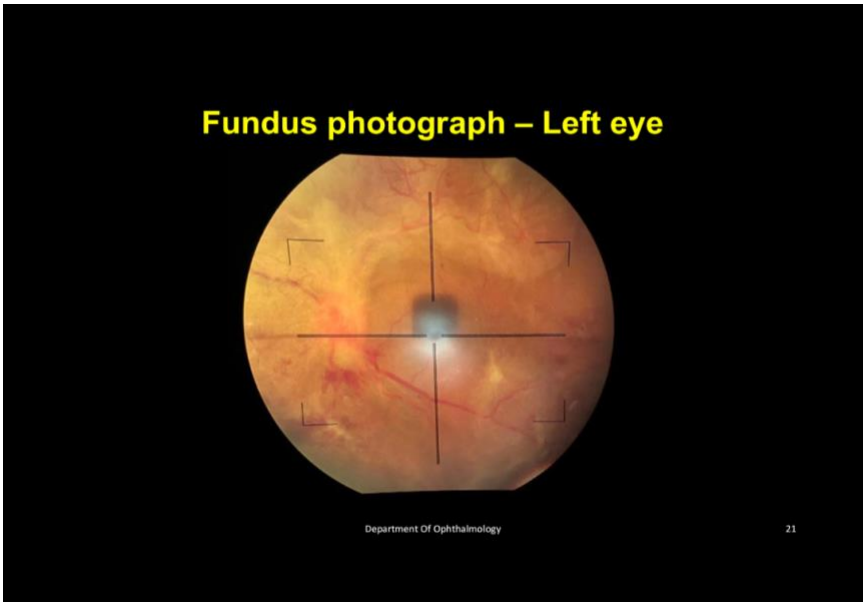


Figure 2: *Fundus photograph of the left eye showing non-proliferative diabetic retinopathy (NPDR) changes with microaneurysms, retinal hemorrhages, and mild arteriolar narrowing.*

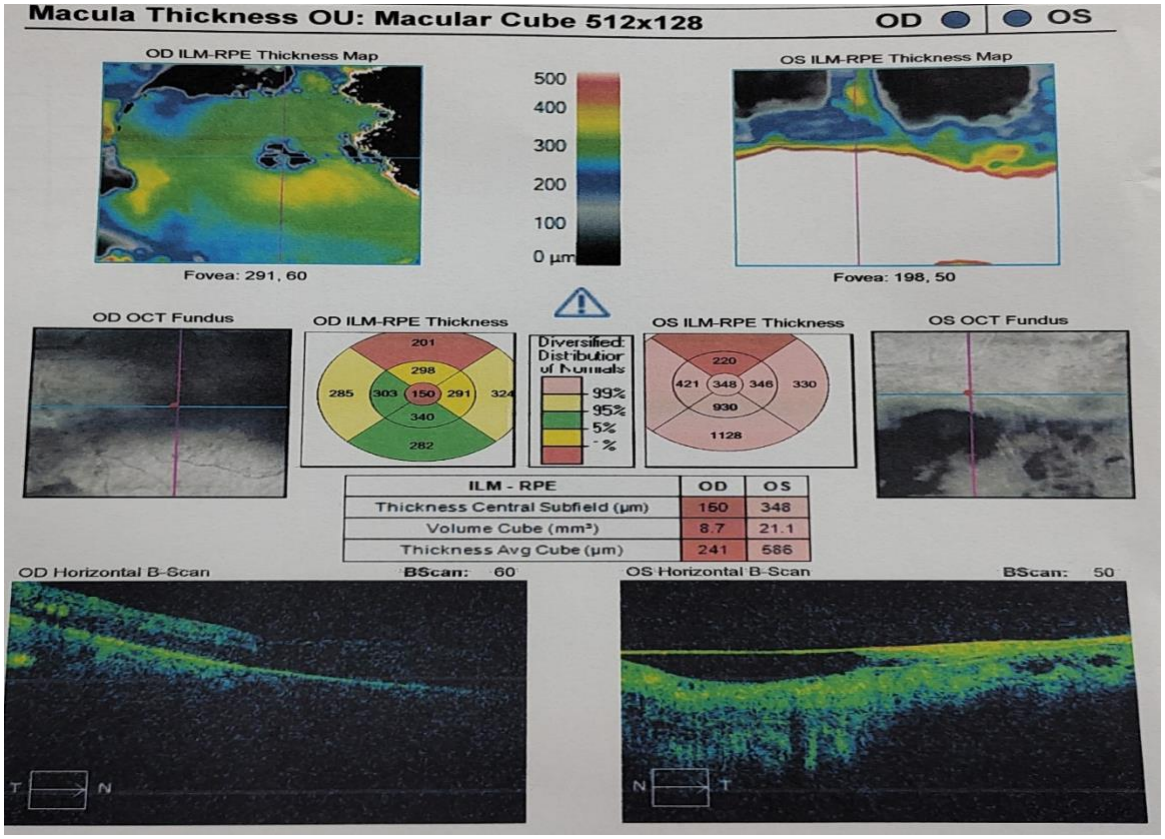


Figure 3: The OCT macular thickness analysis shows **normal thickness in the right eye (OD)** and **macular thickening with probable macular edema in the left eye.**

ANNEXURES –V

MASTER CHART

Key to master chart

IP	In Patient
M	Male
F	Female
RE	Right eye
LE	Left eye
FBS	Fasting blood sugar
PPBS	Post prandial blood sugar

RBS	Random blood sugar
eGFR	Estimated glomerular filteration rate
NPDR	Non proliferative diabetic retinopathy
PDR	Proliferative diabetic retinopathy
ADPKD	Autosomal dominant polycystic kidney disease

Name	Age	Sex	IP No.	Diabetic status	Duration of diabetes	Hypertensive status	Hb A1c	FBS	PPBS	RBS	eGFR	Serum Creatinine	Dialysis status	Duration of Dialysis	Cause of CKD	Fundus findings RE	Fundus findings LE	Subfoveal RE	Subfoveal LE	Superior RE	Superior LE	Inferior RE	Inferior LE	Temporal RE	Temporal LE	Nasal RE	Nasal LE
Chandrkanth Athani	72	M	276181	Yes	12 years	No	7.4	201	287	306	23	3.3	Yes	5 years	Diabetic Nephropathy	Severe NPDR	Severe NPDR	182	188	174	191	172	182	193	190	179	181
Shantabai Chattar	60	F	358828	No		Yes	6.1	108	120	132	21	4.1	Yes	3 years	Hypertensive Nephropathy	Grade II Hypertenisve retinopathy	Grade II Hypertensive retinopathy	230	221	240	234	250	243	219	224	241	244
Danavva Mahajan	80	F	402807	No		No	6.3	104	140	141	18	4.5	Yes	4 years	Bilateral renal artery stenosis	Arteriolar attenuation	Arteriolar attenuation	220	224	239	233	235	213	232	230	212	222
Sagar Nadavinkeri	30	M	25962	Yes	4 years	No	8.1	109	171	140	16	3.8	Yes	6 months	Diabetic Nephropathy	Normal	Normal	288	278	291	288	289	290	285	287	279	290
Kallappa Manur	60	M	12950	Yes	15	No	8.4	120	188	208	20	3.1	Yes	2 years	Diabetic Nephropathy	Moderate NPDR	Moderate NPDR	214	220	216	208	212	208	209	211	206	199
Sumana Talwar	37	F	320156	No		No	6.4	105	144	130	26	2.5	No		Bilateral ADPKD	Normal	Normal	290	287	288	285	279	289	291	295	288	299
Shamshad Sheikh	48	F	70270	No		No	5.6	110	143	156	24	1.8	No		Takayasu arteritis	Grade I Hypertensive retinopathy	Grade I Hypertensive retinopathy	213	212	214	212	220	218	214	208	210	211
Veerangouda Perannavar	62	M	258111	Yes	8 years	Yes	7.6	173	213	233	19	4.2	Yes	8 months	Diabetic Nephropathy	Moderate NPDR	Moderate NPDR	225	221	219	226	230	231	219	224	226	226
Kamalakshi Maled	35	F	9330	No		No	6.4	103	123	132	24	2.1	No		Bilateral renal artery stenosis	Arteriolar attenuation	Arteriolar attenuation	230	231	234	231	233	232	234	236	241	229
Sudhir Sonawane	63	M	176412	Yes	12 years	Yes	7.1	145	211	231	20	1.9	No		Diabetic Nephropathy	Severe NPDR	Severe NPDR	187	179	188	189	186	186	188	196	189	185
Dawalsab Nadaf	75	M	356476	Yes	20	No	7.5	129	231	267	18	3.1	Yes	2 years	Diabetic Nephropathy	Severe NPDR	Severe NPDR	181	178	175	180	181	176	175	179	180	177
Sunanda Walikar	37	F	374169	No		No	5.8	100	121	143	25	1.9	No		Bilateral renal artery stenosis	Normal	Normal	278	276	279	280	284	278	279	281	280	274
Siddalingappa Pujari	77	M	246118	Yes	20 years	No	7.4	155	247	275	16	5.7	Yes	2 months	Diabetic Nephropathy	Severe NPDR	Severe NPDR	176	177	178	170	174	180	179	174	169	178
Sidanna Hadpad	40	M	189760	No		No	6.1	102	122	156	23	1.8	No		Bilateral Hydronephrosis	Normal	Normal	287	289	280	286	290	279	276	289	285	288
Valubai Rathod	45	F	161077	No		No	5.6	103	110	109	25	1.8	No		Bilateral Glomerulonephritis	Normal	Normal	289	278	287	279	285	276	285	279	283	278
Gollalappa Kachabal	60	M	275330	Yes	5 years	Yes	7.2	130	209	204	27	1.7	No		Diabetic Nephropathy	Mild NPDR	Mild NPDR	233	241	232	243	235	246	236	239	240	240
Bhimappa	76	M	153293	Yes	10 years	Yes	7.5	155	250	243	18	2.3	No		Diabetic Nephropathy	Mild NPDR	Mild NPDR	231	239	230	241	233	241	231	234	236	241

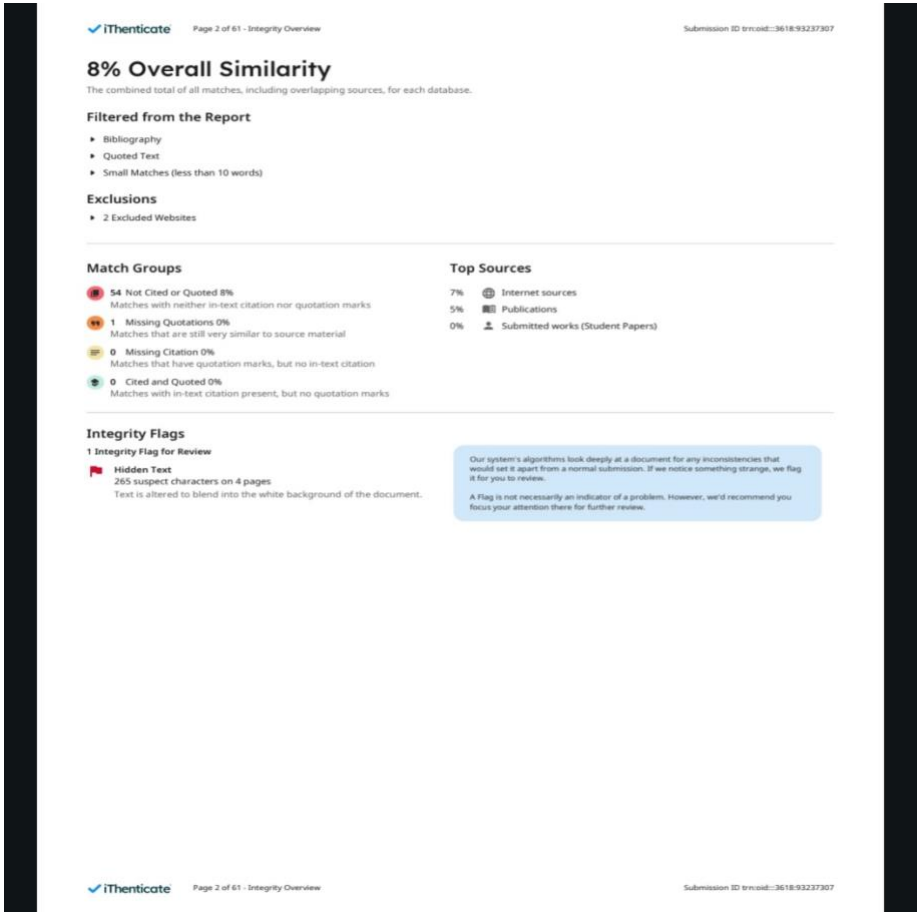
Mahadevi	64	F	228847	No		Yes	5.3	102	143	132	22	2.5	No		Hypertensive Nephropathy	Grade I Hypertensive retinopathy	Grade I Hypertensive retinopathy	240	239	233	231	235	236	233	241	237	236
Parvati Deginal	70	F	16434	Yes	18 years	No	8.9	188	265	238	20	1.9	No		Diabetic Nephropathy	Mild NPDR	Mild NPDR	239	244	245	238	240	241	239	237	243	244
Gurusidhappa	70	M	192532	No		Yes	6.2	102	144	132	22	2.1	No		Bilateral renal artery stenosis	Normal	Normal	277	275	279	280	269	271	273	269	276	275
Sagar Hanamshetti	30	M	25962	Yes	10 years	No	7.1	144	203	200	24	1.7	No		Bilateral Hydronephrosis	Normal	Normal	280	281	283	279	280	277	281	280	283	276
Sidanna Nadvinkeri	63	M	449299	Yes	8 years	No	7	156	231	205	22	1.9	No		Diabetic Nephropathy	Normal	Normal	279	280	280	283	278	278	281	283	278	281
Bhimashi	60	M	21387	No		Yes	5.7	104	150	154	19	2.1	Yes	3 years	Hypertensive Nephropathy	Grade I Hypertensive retinopathy	Grade I Hypertensive retinopathy	210	212	220	213	209	210	213	209	215	208
Suvarna	69	F	115358	No		No	5.6	109	120	122	22	2.5	Yes	1 year	Bilateral renal artery stenosis	Normal	Normal	276	275	269	277	268	270	271	278	268	270
Gurusidappa	70	M	232247	Yes	10 years	No	7.8	155	234	254	18	3.1	Yes	2 years	Diabetic Nephropathy	Moderate NPDR	Moderate NPDR	211	210	209	208	210	211	212	210	209	207
Vaibhav	44	M	248321	No		No	5.6	104	132	134	25	1.6	No		Bilteral glomerulonephritis	Normal	Normal	280	280	281	279	277	279	283	283	281	276
Somaningappa	81	M	11934	Yes	24 years	No	8.3	121	234	256	13	4.5	Yes	4 years	Diabetic Nephropathy	Severe NPDR	Severe NPDR	141	177	139	175	140	169	138	175	137	168
Keerthana	41	F	211476	No		No	5.5	110	120	121	24	1.8	No		Bilateral Hydronephrosis	Normal	Normal	276	279	281	275	277	269	273	270	274	269
Mohan Chavan	35	M	242345	No		Yes	5.8	102	131	152	27	1.8	No		Hypertensive Nephropathy	Normal	Normal	290	291	294	288	289	290	289	286	286	293
Sunanda Bhimshi	59	F	23983	Yes	2 years	Yes	7.9	189	234	278	16	2.5	Yes	1 year	Diabetic Nephropathy	Mild NPDR	Mild NPDR	232	231	229	231	235	240	238	241	232	235
Shantabai Jalamati	68	F	171674	Yes	10 years	Yes	8.2	178	205	244	20	2.2	Yes	2 years	Diabetic Nephropathy	Severe NPDR	PDR	177	174	179	182	174	176	180	173	176	180
Noushad	46	F	397688	No		Yes	5.4	102	110	145	22	1.9	No		Hypertensive Nephropathy	Grade I Hypertensive retinopathy	Grade I Hypertensive retinopathy	200	205	210	208	213	209	207	206	211	213
Somaning Patil	65	M	186182	Yes	12 years	Yes	9.2	188	258	341	15	2.3	No		Diabetic Nephropathy	PDR	PDR	168	165	170	171	163	161	170	167	168	171
Shweta Ahirsang	29	F	186214	No		No	5.3	100	109	104	27	1.9	No		Bilateral Glomerulonephritis	Normal	Normal	277	280	281	276	283	279	284	279	280	281
Shabbir	43	M	408914	No		Yes	5.3	88	103	107	25	1.8	No		Hypertensive Nephropathy	Normal	Normal	299	290	294	289	287	294	300	299	297	304
Sharda Biradar	46	F	408905	Yes	10 years	No	7.6	108	110	134	20	4.1	Yes	1 year	Bilateral renal artery stenosis	Arteriolar attenuation	Arteriolar attenuation	265	259	257	277	276	278	280	268	270	267
Shalubai Chavan	59	F	5627	Yes	5 years	No	8.1	133	206	209	22	3.2	No		Diabetic Nephropathy	Mild NPDR	Mild NPDR	240	238	248	237	239	244	250	248	238	245
Somaning Patil	65	M	9021	Yes	13 years	Yes	7.9	130	209	233	19	3.1	No		Diabetic Nephropathy	Moderate NPDR	Moderate NPDR	220	219	228	226	218	211	214	210	211	208

Gangavva Madar	71	F	48572	No		Yes	6.1	85	100	128	24	2.8	No		Hypertensive Nephropathy	Grade II Hypertensive retinopathy	Grade II Hypertensive retinopathy	191	198	195	189	188	195	200	199	203	204
Rohan Shingade	38	M	65744	No		Yes	5.9	98	103	121	26	1.8	No		Hypertensive Nephropathy	Normal	Normal	289	291	302	300	298	294	289	304	300	301
Meenakshi Sorgavi	77	F	493294	Yes	20 years	Yes	9.5	180	244	287	18	3.3	Yes	2 years	Diabetic Nephropathy	Severe NPDR	Severe NPDR	181	185	188	179	175	183	189	176	182	181
Suvarna Natekar	80	F	45325	Yes	17 years	No	11.4	255	298	304	13	4.3	Yes	3 years	Diabetic Nephropathy	PDR	PDR	167	163	159	158	161	154	149	150	158	153
Mallikarjun	45	M	8732	No		Yes	5.5	89	107	133	23	2.9	No		Hypertensive Nephropathy	Normal	Normal	280	281	278	279	274	283	286	278	281	277
Sunanda Rajput	52	F	56332	No		No	4.7	90	105	123	24	2.3	No		Bilateral renal artery stenosis	Normal	Normal	277	275	267	285	286	278	286	278	287	288
Mukund Rawal	59	M	45456	Yes	10 years	Yes	7.6	101	133	127	24	2.4	No		Diabetic Nephropathy	Mild NPDR	Mild NPDR	244	243	255	254	255	246	251	249	253	255
Sonam	31	F	76974	No		No	4.5	87	101	120	21	2.8	Yes	8 months	Bilateral glomerulonephritis	Normal	Normal	287	290	288	289	291	293	287	295	281	279
Mubasshir	56	M	69460	Yes	7 years	No	7.5	143	188	176	19	3.2	Yes	2 years	Diabetic Nephropathy	Mild NPDR	Mild NPDR	234	240	237	244	236	231	245	247	250	245
Danamma Mahajan	70	F	79593	No		Yes	5.6	90	103	123	24	3.4	Yes	3 years	Hypertensive Nephropathy	Grade II Hypertensive retinopathy	Grade II Hypertensive retinopathy	206	200	201	198	203	199	205	193	205	204
Mudkappa	84	M	3495	Yes	23 years	Yes	7.2	126	144	153	19	4.5	Yes	7 years	Diabetic Nephropathy	Severe NPDR	Severe NPDR	178	181	185	192	188	190	194	183	182	179
Satvik	25	M	9873	No		No	5.4	89	4.5	107	20	3.4	No		Takayasu arteritis	Normal	Normal	289	290	294	286	288	293	285	287	294	287
Nagamma	75	F	85699	Yes	20 years	No	7.4	144	167	165	23	2.4	No		Diabetic Nephropathy	Moderate NPDR	Severe NPDR	230	187	237	194	240	190	236	188	239	179
Tukaram Mashal	80	M	68400	Yes	21 years	Yes	9.5	197	342	365	14	7.4	Yes	2 years	Diabetic Nephropathy	PDR	PDR	177	179	184	183	169	174	178	169	175	170
Mahantesh	65	M	9549	No		Yes	6.8	88	104	127	18	5.8	Yes	6 years	Hypertensive Nephropathy	Grade II Hypertensive retinopathy	Grade II Hypertensive retinopathy	193	190	195	191	188	186	194	184	193	184
Pushkar	51	M	86850	No		No	5.8	94	110	114	24	3.5	No		Bilateral Glomerulonephritis	Normal	Normal	275	277	280	275	281	276	289	274	284	280
Sunanda Thobde	78	F	349294	Yes	18 years	No	7.9	144	178	190	20	4.2	No		Diabetic Nephropathy	Moderate NPDR	Severe NPDR	340	388	295	289	280	301	295	299	293	310
Pirappa	67	M	44895	No		Yes	5.4	83	104	112	18	6.8	No		Hypertensive Nephropathy	Normal	Normal	277	275	280	267	269	278	280	271	280	275
Shivasangamma	74	F	49275	Yes	20 years	Yes	6.1	174	245	277	19	5	No		Diabetic Nephropathy	Severe NPDR	Severe NPDR	177	180	183	174	173	183	181	175	187	175
Mallappa	80	M	46375	Yes	15 years	No	7.8	198	344	329	17	8.4	Yes	2 years	Diabetic Nephropathy	Severe NPDR	Severe NPDR	165	160	164	169	162	170	171	169	164	167
Tushar Lambkane	31	M	8943	No		No	4.5	67	103	100	20	5.6	Yes	1 year	Bilateral Hydronephrosis	Normal	Normal	280	281	278	283	279	278	275	269	281	288

Muskaan	29	F	299341	Yes	8 years	No	7.5	120	139	125	24	6.1	No		ADPKD	Normal	Normal	281	287	89	279	283	280	279	284	285	289
Danamma Shetgar	64	F	75849	No		Yes	5.4	88	108	120	20	4.3	No		Hypertensive Nephropathy	Grade I Hypertensive retinopathy	Grade I Hypertensive retinopathy	230	227	229	234	240	239	241	235	229	237
Keerti	38	F	4958	Yes	5 years	No	7.4	133	188	191	22	3.4	Yes	2 years	Diabetic Nephropathy	Normal	Normal	287	280	279	284	279	283	285	280	277	287
Sangeeta Natikar	58	F	382945	No		Yes	4.5	83	101	110	20	4.3	Yes	2 years	Hypertensive Nephropathy	Normal	Normal	285	289	273	275	276	277	279	283	285	286
Malkappa	60	M	48939	Yes	12 years	No	8.9	178	349	304	13	7.8	No		Diabetic Nephropathy	PDR	PDR	169	170	173	169	174	177	173	169	180	163
Prashant	36	M	38402	No		No	5.3	99	103	140	19	7.3	No		Bilateral Glomerulonephritis	Arteriolar attenuation	Arteriolar attenuation	230	234	229	238	230	235	229	227	234	235
Somaningappa	59	M	394752	Yes	15 years	No	7.9	140	204	210	21	6.5	Yes	4 years	Diabetic Nephropathy	Severe NPDR	Severe NPDR	184	179	188	173	183	187	179	174	169	180
Vinayak Patil	44	M	201199	No		No	5.4	94	109	104	25	4.3	No		Bilateral renal artery stenosis	Normal	Normal	284	278	279	281	280	274	279	283	281	288
Devaki Naik	49	F	34892	Yes	7 years	No	8.4	149	199	187	20	4.5	No		Diabetic Nephropathy	Mild NPDR	Mild NPDR	239	243	245	244	237	250	247	240	231	244
Basavraj Angadi	61	M	45892	No		Yes	5.3	84	99	103	21	3.3	No		Hypertensive Nephropathy	Grade I Hypertensive retinopathy	Grade I Hypertensive retinopathy	203	205	199	210	223	234	202	220	215	224
Nishant	25	M	399402	No		No	5.4	94	103	120	20	3.2	No		Bilateral focal Glomerulosclerosis	Normal	Normal	284	284	289	287	278	290	285	289	276	280
Mudkanna Patanshetti	54	M	48294	Yes	6 years	No	7.9	133	237	267	17	4.4	Yes	1 year	Diabetic Nephropathy	Moderate NPDR	Moderate NPDR	214	218	220	215	220	217	230	229	213	220
Meenakshi Budihal	56	F	7649	No		No	6.4	102	110	111	24	3.8	No		Lupus Nephritis	Arteriolar attenuation	Arteriolar attenuation	269	265	270	274	69	274	265	278	280	281
Mihir	29	M	293941	No		No	5.3	94	103	120	20	4	No		HUS	Normal	Normal	277	279	273	275	269	279	272	274	275	280
Sangamesh Halikatti	65	M	39485	Yes	5 years	No	8.4	134	201	240	19	8.4	Yes	2 years	Diabetic Nephropathy	Severe NPDR	Severe NPDR	170	175	179	181	183	173	179	188	184	175
Ambavva Naik	70	F	472930	No		Yes	4.9	99	104	109	16	7.4	No		Hypertensive Nephropathy	Grade I Hypertensive retinopathy	Grade I Hypertensive retinopathy	250	245	249	261	271	270	269	265	270	274
Nilamma Choudhari	66	F	109072	Yes	10 years	Yes	8.5	194	344	207	12	10.3	Yes	1 year	Diabetic Nephropathy	Severe NPDR	Severe NPDR	176	177	169	173	167	180	176	173	179	180

Annexure VI

Plagiarism report



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