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STRUCTURAL OCT BIOMARKERS OF DIABETIC RETINOPATHY PROGRESSION: ROLE OF CSME AND DRIL IN PREDICTING VISUAL OUTCOMES

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ABSTRACT

Background

Diabetic retinopathy (DR) is a major cause of vision loss worldwide. [1,2] Structural changes such as clinically significant macular edema (CSME) and disorganization of the retinal inner layers (DRIL), detectable by optical coherence tomography (OCT), have emerged as important biomarkers in predicting visual outcomes. Understanding their distribution across DR stages and their combined impact on visual acuity can enhance clinical decision-making. [3,4]

Aims

To evaluate the prevalence of CSME and DRIL in patients with diabetic retinopathy, assess their distribution across different DR stages, and analyze their correlation with visual acuity.

Methods

A cross-sectional observational study was conducted at the Department of Ophthalmology, Government Medical College (GMC), Palakkad, from November 2024 to April 2025. A total of 100 diabetic retinopathy patients were included based on clinical diagnosis and OCT findings. DR severity was graded according to standard fundus examination criteria. OCT was used to assess the presence of CSME and DRIL. Visual acuity was measured using Snellen's chart. Data were tabulated and analyzed to explore the distribution of DRIL and CSME in different DR stages and to assess their correlation with visual acuity.

Results

Out of 100 patients, CSME was present in 34%, and DRIL in 31%, with increasing prevalence in severe NPDR and PDR stages. Around 20% of patients had both CSME and DRIL. Among these, 85% exhibited moderate to severe visual acuity loss (≤6/36). DRIL and CSME were more frequently associated with advanced DR stages and poorer visual function.

Conclusion

The presence of DRIL and CSME correlates strongly with disease severity and visual acuity in diabetic retinopathy. Their identification through OCT imaging offers valuable prognostic insights and can aid in individualized treatment planning for diabetic patients at risk of vision loss.

Keywords: Diabetic Retinopathy, DRIL, CSME, Visual Acuity, OCT, GMC Palakkad.

INTRODUCTION

Diabetic retinopathy (DR) is a microvascular complication of diabetes mellitus and one of the leading causes of preventable blindness in the working-age population worldwide.[5] With the global rise in

diabetes prevalence, the burden of DR is expected to increase significantly, especially in low- and middle-income countries like India. Early identification of biomarkers associated with disease progression and visual impairment is crucial for timely intervention and prevention of irreversible vision loss.[2]

Among the sight-threatening complications of DR, clinically significant macular edema (CSME) represents a major cause of central vision loss.[6] CSME results from the breakdown of the blood-retinal barrier and accumulation of fluid in the macula, leading to retinal thickening and photoreceptor dysfunction. The advent of high-resolution optical coherence tomography (OCT) has revolutionized the evaluation of macular pathology, allowing detailed assessment of retinal layers and quantification of macular edema.[7]

Recently, Disorganization of Retinal Inner Layers (DRIL) has emerged as a novel structural OCT biomarker with significant prognostic value. First described by Sun et al. [4] DRIL refers to the loss of identifiable boundaries between the ganglion cell–inner plexiform layer complex, inner nuclear layer, and outer plexiform layer. DRIL is increasingly recognized as a marker of neuroretinal disruption and has been shown to correlate strongly with poor visual acuity, independent of central retinal thickness.[8]

Understanding the distribution of CSME and DRIL across various stages of diabetic retinopathy and their impact on visual acuity can help clinicians stratify patients based on risk and predict treatment outcomes more effectively.[9] While several studies have explored these parameters in tertiary centers, there is a paucity of data from peripheral government institutions in India, where patient demographics and access to care may differ.

This study was conducted at Government Medical College (GMC), Palakkad, with the aim of evaluating the prevalence of CSME and DRIL in patients with diabetic retinopathy, analyzing their distribution across different DR stages, and correlating these findings with visual acuity outcomes. The results of this study may provide useful insights into disease behavior in a real-world, semi-urban clinical setting and support the role of OCT biomarkers in routine DR management.

MATERIALS AND METHODS

Study Design and Setting

This was a cross-sectional observational study conducted in the Department of Ophthalmology, Government Medical College (GMC), Palakkad, Kerala. The study was conducted after obtaining approval from the Institutional Ethics Committee. The study was carried out over a period of six months, from November 2024 to April 2025.

Study Population

A total of 100 patients diagnosed with diabetic retinopathy were included in the study. Patients attending the ophthalmology outpatient department who met the inclusion criteria were enrolled consecutively.

Inclusion Criteria

- Patients aged ≥18 years with a clinical diagnosis of Type 2 Diabetes Mellitus
- Fundus findings consistent with diabetic retinopathy (any stage)
- Willingness to undergo OCT evaluation
- Provided informed consent to participate in the study

Exclusion Criteria

- Presence of other retinal diseases (e.g., retinal vein occlusion, AMD)
- Previous laser treatment or intravitreal injections
- History of ocular surgery within the past 6 months
- Media opacities precluding good-quality OCT imaging

Clinical Evaluation

Each patient underwent a comprehensive ophthalmic evaluation, including:

- Visual acuity measurement using Snellen's chart.
- Slit-lamp biomicroscopy.
- Intraocular pressure measurement.
- Dilated fundus examination using indirect ophthalmoscopy and +90D lens.
- Grading of diabetic retinopathy was done based on ETDRS classification into:
  - Mild NPDR
  - Moderate NPDR
  - Severe NPDR
  - Early PDR
  - High-risk PDR

OCT Imaging and Biomarker Assessment

Spectral-domain Optical Coherence Tomography (SD-OCT) was performed using Zeiss Cirrus HD-OCT to assess:

- Presence and extent of clinically significant macular edema (CSME)
- Identification of Disorganization of Retinal Inner Layers (DRIL), defined as the loss of clear boundaries between the ganglion cell-inner plexiform layer, inner nuclear layer, and outer plexiform layer in the central 1-mm zone of the macula.

Data Collection and Analysis

- Patients were grouped based on DR stage and presence of CSME and/or DRIL.
- Data were entered into Microsoft Excel and analyzed using SPSS version XX (or any other software used).
- Descriptive statistics (mean, standard deviation, percentages) were used.
- Associations between DR stage, CSME, DRIL, and visual acuity were analyzed using chi-square test, ANOVA, or t-test as appropriate.
- A p-value < 0.05 was considered statistically significant.

RESULTS

This study analysed data from 100 patients diagnosed with Type 2 Diabetes and CSME.

Demographic and Clinical Profile

The mean age of the patients was 56.25 ± 5.83 years. The majority of patients were in the 50-70 years age bracket. The duration of diabetes was a key factor, with nearly half the patients having the disease for over 16 years. Key demographic data are summarized in Table 1.

Characteristic		**Number of Patients**	**Percentage**
Age Group	30–49 years	26	26.0%
	50–70 years	74	74.0%
Gender	Male	66	66.0%
	Female	34	34.0%
Duration of Diabetes	< 5 years	7	7.0%
	6–10 years	18	18.0%
	11–15 years	28	28.0%
	> 16 years	47	47.0%

Table 1: Demographic and Clinical Profile of Patients

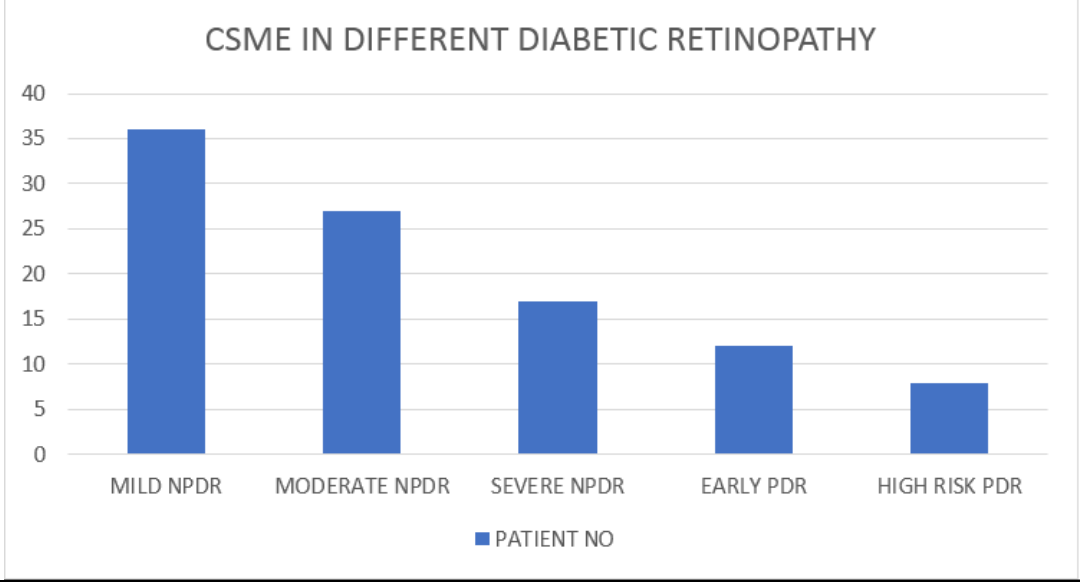
Severity of Diabetic Retinopathy

Patients were categorized based on the ETDRS grading for diabetic retinopathy. A substantial portion of patients with CSME (37%) already had advanced stages of retinopathy (Severe NPDR or PDR). The distribution is detailed in Table 2.

DR Stage	Patient No	Percentage
Mild NPDR	36	36%
Moderate NPDR	27	27%
Severe NPDR	17	17%
Early PDR	12	12%
High Risk PDR	8	8%

Table 2: Distribution of Diabetic Retinopathy Severity (N=100)

This is a graphical representation of the prevalence of Clinically Significant Macular Oedema (CSME) across different grades of Diabetic Retinopathy (DR) in a study cohort of 100 patients. CSME prevalence rises progressively with DR severity, reflecting the increased retinal vascular leakage and macular involvement seen in more advanced stages. The highest proportion of CSME is observed in early and high-risk proliferative stages.

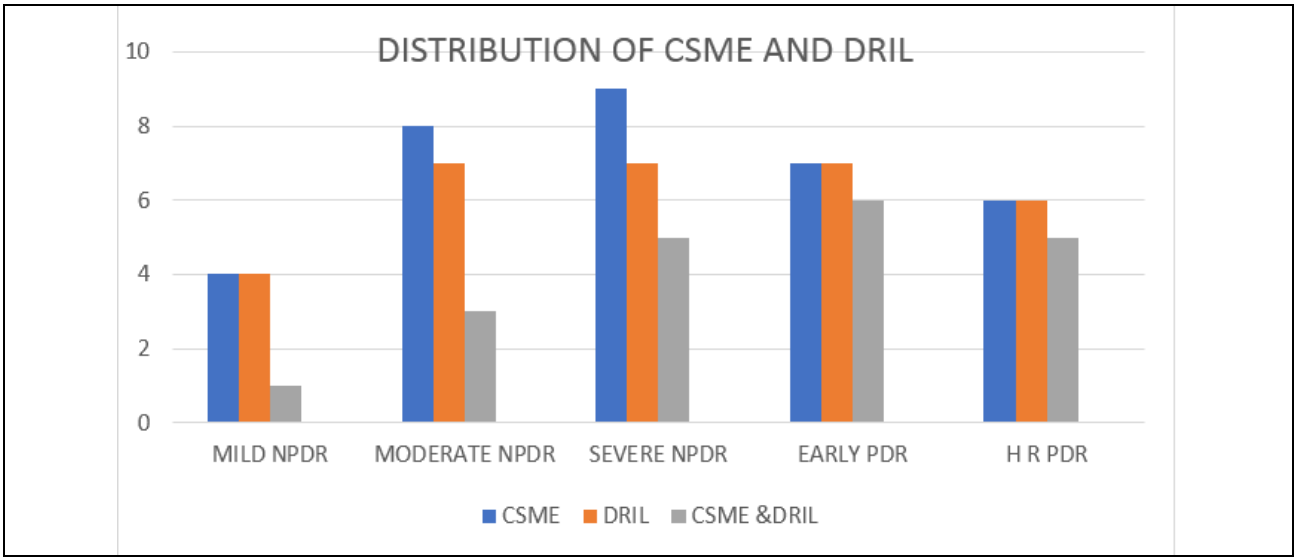


Graph 1: Distribution of CSME in Different DR Stages

DR Stages	No of DRIL Patients	DRIL %
Mild NPDR	4	10%
Moderate NPDR	7	25%
Severe NPDR	7	40%
Early PDR	7	60%
High risk PDR	6	75%

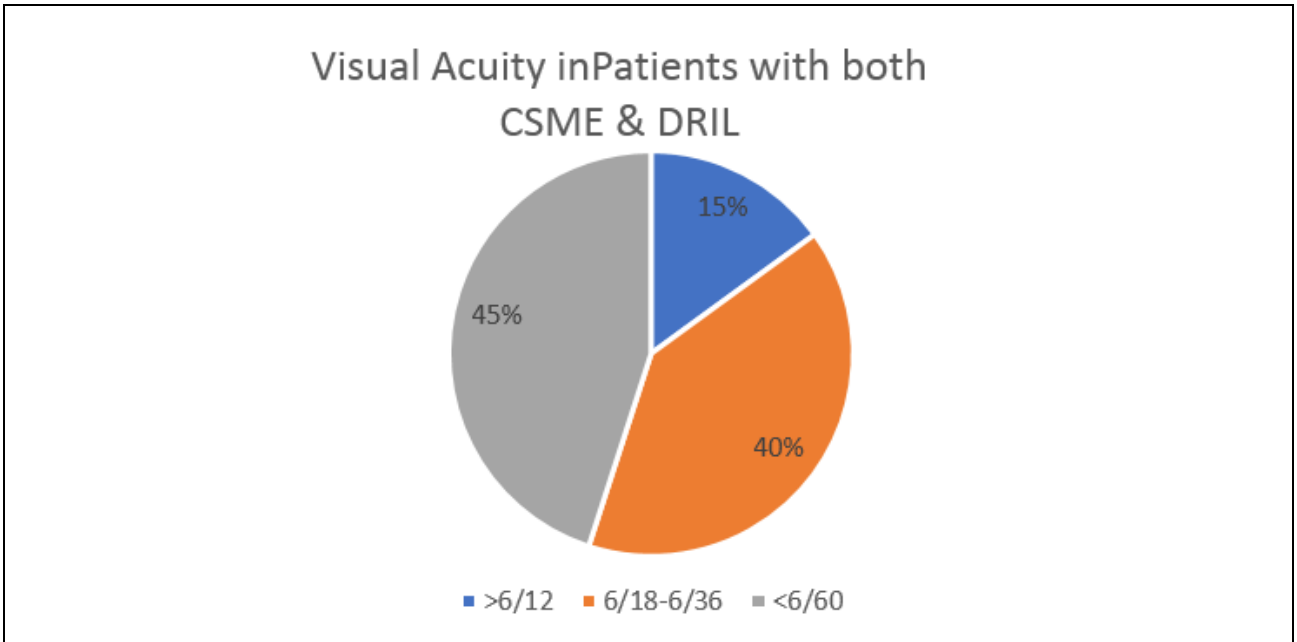
Table 3: Distribution of DRIL in Different DR Stages

This table demonstrates the estimated frequency of Disorganization of Retinal Inner Layers (DRIL) across the spectrum of DR severity. DRIL is an OCT biomarker that signifies structural disarray in the inner retina and has been linked to poor visual outcomes. The estimates here align with known pathophysiological patterns-DRIL incidence increases significantly from mild NPDR to high-risk PDR, corresponding to the increasing ischemic and neurodegenerative burden in diabetic eyes.



Graph 2: CSME with DRIL in Different DR Stages

This graph identifies the estimated number of patients who have both CSME and DRIL, which is a clinically important subgroup due to their high risk for visual impairment. The overlap is minimal in early stages but becomes more significant in severe NPDR and PDR. The presence of DRIL in patients with CSME may suggest chronicity, neurodegeneration, and worse anatomical disruption, which can adversely affect treatment outcomes and prognosis.



Graph 3

This pie chart displays the distribution of visual acuity among patients with both CSME and DRIL. The majority (85%) experienced moderate to severe vision loss, supporting the role of DRIL as a biomarker of poor visual prognosis in the presence of macular edema.

DISCUSSION

This study provides crucial insights into the progression of diabetic retinopathy and its direct impact on visual function. The primary conclusion is the robust and statistically significant association between the severity of DR, manifesting as CSME, and the decline in visual acuity.[10]

The demographic profile of our study population, with a mean age of 56.25 years, aligns with findings from numerous other studies. This reinforces that CSME is predominantly a disease of the middle-aged and elderly. One of the most critical risk factors for the development of DR and CSME is the

duration of diabetes.[11] Our study strongly supports this, revealing that 47% of patients with CSME had a diabetes duration of over 16 years.

A pivotal finding of this study is the profound negative impact of the Disorganisation of Retinal Inner Layers (DRIL) on visual acuity. DRIL represents a state of neurodegeneration where the distinct laminar architecture of the retina is lost, impairing the transmission of visual signals.[12] Our results, which show that 100% of patients with DRIL had moderate or severe visual loss, are consistent with a growing body of evidence that identifies DRIL as a more reliable predictor of poor visual outcome than central retinal thickness alone. The presence of DRIL suggests that the retinal damage has progressed beyond simple edema to involve irreversible neuroretinal cell death, which explains why vision may remain poor even after macular edema resolves.[4] Studies have also shown that DRIL is associated with neuroretinal dysfunction even in the early stages of diabetic retinopathy. [12,13]

The pathophysiology of DME is complex, driven primarily by the overexpression of Vascular Endothelial Growth Factor (VEGF) in response to retinal ischemia, which increases vascular permeability.[14] Inflammation also plays a critical role. The presence of hard exudates, a key feature in the patients studied, signifies this chronic vascular leakage and is a known marker for potential photoreceptor damage.[15]

The strength of the correlation between visual acuity and macular edema ($p<0.0005$) is the cornerstone of our results. As retinal tissue thickens and fluid accumulates in the macula, the precise arrangement of photoreceptor cells is disrupted, leading to blurred and distorted vision. The fact that two-thirds of the patients had moderate visual impairment and nearly one-third had severe visual impairment highlights the advanced stage at which many patients present to tertiary care centers.

Finally, our study indicated that the underlying pathogenic mechanisms are driving macular edema, the broader progression of retinopathy, and the development of DRIL, and they are intrinsically linked.

SUMMARY & CONCLUSION

This study underscores the clinical importance of evaluating both vascular and neurodegenerative changes in diabetic retinopathy using optical coherence tomography (OCT). We observed that the prevalence of clinically significant macular edema (CSME) and disorganization of the retinal inner layers (DRIL) increased progressively with the severity of diabetic retinopathy (DR). While CSME is a well-established marker of macular thickening due to vascular leakage, DRIL represents a relatively newer OCT biomarker that reflects disruption of the inner retinal microarchitecture, likely due to ischemia or neurodegeneration.

The presence of DRIL alone, and more significantly when combined with CSME, was strongly associated with poor visual outcomes. In our cohort, 85% of patients with both CSME and DRIL had moderate to severe visual impairment. This finding highlights the synergistic effect of these two structural changes on visual function and reinforces the need for their combined assessment during patient evaluation.

OCT, a non-invasive and widely accessible imaging modality, enables clinicians to go beyond macular thickness measurements and examine deeper structural alterations like DRIL. [16,17] Identifying these biomarkers early in the course of DR can aid in stratifying patients at higher risk of vision loss, enabling more aggressive monitoring, earlier intervention, and potentially better outcomes.

In conclusion, this study adds to the growing evidence that DRIL is a valuable marker of retinal dysfunction and visual prognosis in diabetic retinopathy. Routine OCT assessment of both CSME and DRIL should be integrated into standard diabetic eye care protocols. Further longitudinal studies with larger sample sizes and quantitative measurements are warranted to validate these findings and explore their predictive value over time.

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