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ORIGINAL ARTICLE

A HOSPITAL-BASED STUDY ON THE INFLUENCE OF SYSTEMIC RISK FACTORS IN THE DEVELOPMENT OF CENTER-INVOLVING MACULAR EDEMA IN PATIENTS WITH DIABETIC RETINOPATHY

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Abstract

Background: Diabetic retinopathy and center-involving diabetic macular edema are the major causes of vision loss in working age individuals, with macular edema resulting from fluid accumulation in the macula leading to increased retinal thickness and visual deterioration.

Objective: To determine the frequency of center-involving diabetic macular edema (Ci-DME) and evaluate its association with glycemic control and serum lipid profile among patients with diabetic retinopathy.

Material and Methods: In this hospital-based analytical cross-sectional study, 200 eyes of 100 diabetic patients were investigated from March 2023 to October 2023 in KGN TH eye department Bannu, Pakistan. The patients were placed into two groups: (1) Ci-DME (DR and Ci-DME coexisting in one or both of the eyes) and group (2) Non-Ci-DME (DR present with or without DME but no Ci-DME in any of the eyes present).The levels of urine albumin, glycosylated hemoglobin (HbA1C) (0.326), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG), and serum total cholesterol have been measured in both groups(>0.272).

Results: 40 (40%) of the 100 diabetic patients were diagnosed with ci-DME, of which 27 (67.27%) were male and 13(32.73%) were female in which high cholesterol level and insufficient glycemic control were significantly correlated. Additionally patients with ci-DME had lower levels of HDL (0.91p) and TG (0.93P), both of which are known risk factors for cardiovascular disease. Despite these distinctions, the differences in lipid levels between the two groups were not statistically significant in this investigation except low density lipoproteins.

Conclusion: Ci-DME is associated significantly with higher level of total cholesterol and poor glycemic control.

Keywords: Center involving Diabetic Macular Edema(Ci-DME), Diabetic retinopathy and Glycosylated Hemoglobin (HbA1C)
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Introduction:

The most common cause of visual impairment in diabetic patients are diabetic retinopathy and diabetic macular edema affecting 1/3rd of patients globally and increases as the age advances.[1, 2]Macular edema is fluid accumulation in the macula, or central part of the retina, experiencing symptoms such as metamorphopsia, micropsia, blurred vision, central scotoma, and reduced contrast or color Sensitivity.3According to the early treatment diabetic retinopathy study (EDRS), clinically significant macular edema (CSME) is defined as retinal thickening or exudates within 500 µm of the center of the macula, or thickening of ≥1 disc diameter from the center of macula.[4]

The clinical entities of center-involving DME (Ci-DME) and non-center-involving DME (Non-Ci-DME) for

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assessing macular edema were later approved by the International Council of Ophthalmology (ICO) in their guidelines for diabetic eye treatment in 2018.[5]
This is the classification:

Center-involving DME: Macula-related retinal thickening involving the central subfield zone (1 mm in diameter)

Non-center involving DME: Macula-related retinal thickening that excludes the central subfield zone (1 mm in diameter) A number of seminal research have demonstrated that strict blood pressure and glucose management can significantly slow the onset and progression of DR.[6] It is unclear, therefore, how lipids contribute to the pathophysiology of DR and CSME.[7]Smoking and albuminuria are positively correlated with DR,[8] although research on their contributions to the development of Ci-DME is lacking. The goal of this research is to ascertain how some potential systemic risk variables, such as albuminuria, hypertension, lipid profile, glycemic management and smoking, affect DR patients with or without Ci-DME and the null hypothesis is that there is no significant association between systemic factors and the occurrence of diabetic macular edema.

Material and Method:

Study Design: This study was a hospital-based analytical cross-sectional study.

Ethics: Patients were informed and consent were signed before participation and all treatments were carried out in compliance with the Declaration of Helsinki's tenets.

This study was conducted in the Department of Ophthalmology, Khalifa Gul Nawaz Teaching Hospital, Bannu, Pakistan, from March 2023 to October 2023. Ethical approval was obtained from the Ethical Review Board (ERB) of Bannu Medical College (ERB No. 43/Dir&Mj/BMC/2024), dated 23 April 2024.

Sample size:200 eyes of 100 patients were included in the research.

µg/min (American Diabetes Association 2013).[9] The (Graph 1) outlines the thresholds for categorizing albumin thresholds and lipid levels which helps in identifying abnormal albumin and lipid levels based on specific thresholds.

Assessment of hypertension: Each patient's blood pressure were assessed and if It was 140/90 mmHg or high were considered hypertensive or if they had used any antihypertensive drugs.

Hypertension can be divided into two stages.

Stage 1, Systolic120-129 mmHg and Diastolic < 80 mmHg

Stage 2, Systolic≥ 140 mmHg and Diastolic ≥ 90 mmHg

Smoking history: Information regarding past and present smoking and non-smoking histories were obtained.

Procedure: Following a thorough history and examination of the anterior segment, the pupil was dilated and a thorough posterior segment examination was performed. The posterior segment was inspected while using a slit-lamp biomicroscope, 78D/90D condensing lenses and to classify diabetic retinopathy an International Clinical Diabetic Retinopathy severity scale. The evaluation of diabetic macular edema (DME) was defined using the methodology of the International Council of Ophthalmology.

Inclusion criteria: Those who met the Ci-DME requirements were assigned to Group-I, also known as the Ci-DME group.

Age (Above 50 years)
Diabetes (Type-1 and Type-II)
Visual impairment
Confirmed by OCT

Exclusion criteria : For research purposes, individuals with any DR grade who did not meet the Ci-DME requirements were allocated to Group II, commonly known as the Non-Ci-DME group, and would be omitted from the study.

Statistical Analysis: To do statistical analysis, data were imported into SPSS version 22. When necessary, the chi-square and Fisher's exact tests were employed, with a significance threshold of $p < 0.05$.

Results:

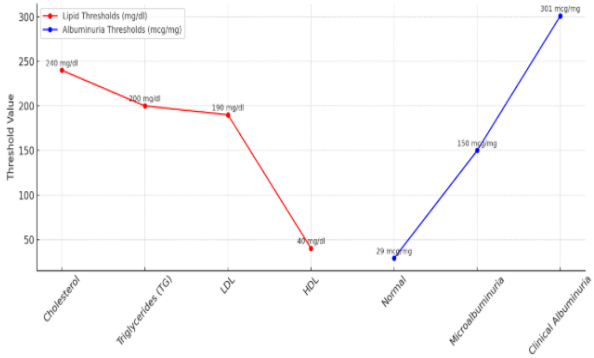
Operational Definitions:

Blood sugar control assessment:

The HbA1C values were measured to assess blood sugar regulation. A common value system was used i.e. Diabetes Control and Complications Trial (DCCT), even if there are several grade methods. 9

Diabetic nephropathy and Lipid profile Assessment:

Diagnosis of albumin in urine was made when albumin excretion rates were more than 200.



Graph I. Lipid Profile and Albuminuria Thresholds

Table 1. Blood Sugar Control Assessment

Category	HbA1C Range	Description
Normal	4.2 - 6.2%	Indicates normal glycemic control

Good	6.3 - 6.8%	Indicates good glycemic control
Fair	6.9 - 7.6%	Indicates fair glycemic control
Poor	>7.6%	Indicates poor glycemic control

Two hundred eyes from one hundred individuals with diabetic retinopathy, whose mean age was 53.5±10.8, were included in our study. 36% of the sample population with DR had Ci-DME, and the male to female ratio was nearly 2:1, with males being impacted more (67.27%) than females (32.73%) as shown in Table 2.

Table 2. Patient Demographics and Clinical Characteristics		
Characteristics	Details	
Sample size	100 patients	200 eyes
Mean Age	53.5 ± 10.8 years	
Gender Distribution	Males: 7.27%	Females: 32.73%
Prevalence of Ci-DME	36% of DR patients	
Severity of Ci-DME	Most had severe NPDR	

The majority of Ci-DME patients in our survey exhibited severe non-proliferative diabetic retinopathy (NPDR). Ci-DME was statistically significantly associated with high blood cholesterol levels and poor glycemic control ($p<0.05$). Our Ci-DME patients had low HDL and high LDL and TG values, and our analysis found no correlation between albuminuria and an elevated risk of Ci-DME. Also no statistical significance was found between hypertension, smoking, and Ci-DME as shown in **Error! Reference source not found.**.

Table 3.Association of Various Factors with Ci-DME		
Factor	**Finding**	**Statistical Significance**
Glycemic Control (HBA1c)	Poor glycemic control associated with Ci-DME	< 0.05
Serum Cholesterol	High levels associated with Ci-DME	<0.05
LDL	Elevated in Ci-DME patients	0.001
Triglycerides (TG)	Elevated in Ci-DME patients	0.93
HDL	Low levels in Ci-DME patients	0.91
Albuminuria	No association with increased risk of Ci-DME	0.6
Hypertension	No statistical significance found with Ci-DME	0.4
Smoking	No statistical significance found with Ci-DME	0.2

Chi-Square test, Fisher exact test used.

Discussion:

Our patients were between the ages of 26 and 80, with a mean age of 53.5 ±10.8 years, which was similar to earlier research. [3] More men (67.27%) than women (32.73%) were impacted. Other investigations have shown similar findings, [6, 7] Nonetheless, some research revealed a female preponderance.[9,10] DR has no sex preference, according to this conclusion. We discovered that Ci-DME was present in 36% of the sample group with DR. This was more than what other studies had previously shown. Our study's greater frequency of Ci-DME may be due to patients low socioeconomic backgrounds, poorly managed diabetes, and delayed therapy.

Our research was carried out at a tertiary care hospital, where comorbidities, poverty, and late presentation are more common than in the general population or peripheral hospitals.

The majority of Ci-DME patients in our research exhibited severe NPDR. Other research showed similar findings. [11] This implies that the two share the same pathogenic route. Ci-DME and inadequate glycemic control were revealed to be statistically significantly correlated ($p <0.05$). Similar findings have been reported in other investigations.[12,13,14]Ci-DME and elevated blood cholesterol levels were shown to be significantly correlated in our investigation, which is in line with previous findings.[15, 16]

In our Ci-DME patients, HDL levels were low while LDL and TG levels were high and there was statistically significant difference between LDL and TG levels. Several studies have found a substantial correlation between Ci-DME and higher levels of total cholesterol and LDL.[17] In our investigation, albuminuria did not correlate with a higher incidence of Ci-DME. Additional research indicates a favorable correlation.[18]Since Microalbuminuria may develop prior to the detection of gross albumin in urine, evaluation of micro albumin instead of urine's albumin may be more sensitive.Ci-DME, smoking, and hypertension did not significantly correlate, as in previous research. [9]Conversely, research like DCCT (1993) and WESDR (1998)6 has suggested that they are linked to a higher risk of DR development. The outcomes are contradictory as a result. The vasodynamic alterations caused by sorbitol buildup and pericyte loss in retinal capillaries may account for a correlation between poor glycemic management and Ci-DME.[19] Similarly, endothelial cell injury may be the cause of a correlation between Ci-DME and elevated total blood cholesterol which lead to endothelial dysfunction by triggering a local inflammatory response, which in turn triggers the production of growth factors and cytokines. [21, 22, 23, 24]

The concept of Ci-DME is important as it often represents the more severe form of the disease that can lead to blindness. [25]Assessing risk factors can guide us towards therapy by assisting in the analysis of predisposing circumstances.

Conclusion:

Ci-DME is significantly correlated with high blood total cholesterol levels and poor glycemic management. Comparing patients with Ci-DME to those with non-Ci-DME who had low HDL levels and high LDL & TGs, no statistically significant differences were found. To aid in the development of methods to prevent or limit the progression of ci-DME more research with great amount of participants is required.

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