



## Original Research Article

# MONOCYTE TO HIGH-DENSITY LIPOPROTEIN RATIO: A NEW NON-INVASIVE SCREENING BIOMARKER FOR PREDICTING DIABETIC RETINOPATHY AND ITS SEVERITY IN TYPE 2 DIABETES MELLITUS PATIENTS

Nikhil Pursnani<sup>1</sup>, Prabhat Kumar Agrawal<sup>2</sup>, Komal<sup>3</sup>, Tirupati Nath<sup>4</sup>, Gunjan Prakash<sup>5</sup>, Kamna Singh<sup>6</sup>, Mridul Chaturvedi<sup>7</sup>

<sup>1</sup>Professor, Department of Emergency Medicine, S.N. Medical College, Agra, India.

<sup>2</sup>Professor, P.G. Department of Medicine, Sarojini Naidu Medical College, Agra, India.

<sup>3</sup>Senior Resident, P.G. Department of Medicine, Sarojini Naidu Medical College, Agra, India.

<sup>4</sup>Professor, Department of Ophthalmology, Sarojini Naidu Medical College, Agra, India.

<sup>5</sup>Professor, Department of Ophthalmology, FH Medical College, Etmadpur, India.

<sup>6</sup>Associate Professor, Department of Biochemistry, FH Medical College, Etmadpur, India.

<sup>7</sup>Professor, P.G. Department of Medicine, Sarojini Naidu Medical College, Agra, India.

Received : 11/03/2026  
Received in revised form : 20/04/2026  
Accepted : 05/05/2026

### Corresponding Author:

**Dr. Komal,**

Senior Resident, P.G. Department of Medicine, Sarojini Naidu Medical College, Agra, India.

Email: komalchaudhary15094@gmail.com

DOI: 10.70034/ijmedph.2026.2.352

Source of Support: Nil,

Conflict of Interest: None declared

**Int J Med Pub Health**

2026; 16 (2); 2109-2112

### ABSTRACT

**Background:** Diabetic retinopathy, is a known microvascular complication of Type2 diabetes mellitus, is a leading cause of avoidable blindness. The monocyte to high-density lipoprotein cholesterol ratio has emerged as a new non invasive, screening biomarker for early detection and intervention. **Objectives:** To evaluate the correlation between Monocyte to High density Lipoprotein ratio for screening and predicting the severity of Diabetic retinopathy in patients with Type 2 diabetes mellitus.

**Materials and Methods:** This observational cross-sectional study included 186 Type 2 diabetes mellitus subjects at outdoor department of tertiary and teaching care centre. Comprehensive ophthalmological evaluation and fundus photography were used to classify patients into no-DR, mild non-proliferative diabetic retinopathy, moderate non-proliferative diabetic retinopathy, severe non-proliferative diabetic retinopathy and proliferative diabetic retinopathy groups. Monocyte count & HDL levels were used to calculate Monocyte to High density Lipoprotein ratio.

**Results:** The Diabetic Retinopathy group showed high mean Monocyte to HDL Ratio in comparison with non-DR ( $p < 0.001$ ). Monocyte to HDL Ratio showed a graded increase with the severity of retinopathy. Multivariate logistic regression indicated Monocyte to HDL Ratio as an independent predictor of Diabetic Retinopathy after adjusting for confounding variable.

**Conclusions:** Monocyte to High density Lipoprotein ratio is directly proportional and strongly associated with both the presence and severity of Diabetic Retinopathy in Type2 Diabetes mellitus patients, showing its future usefulness as a simple, non- invasive, cost-effective biomarker for early Diabetic Retinopathy screening in the areas where resources are limited.

**Keywords:** Diabetic Retinopathy, Monocyte to HDL Ratio, Inflammatory Marker, Type 2 Diabetes Mellitus, Biomarker.

## INTRODUCTION

Type 2 diabetes mellitus (T2DM) is primarily characterized by insulin resistance in peripheral tissues & an insufficient release of insulin secretion from pancreatic  $\beta$ -cells. This research is done to

find out various possible need for early detection strategies and predictive biomarkers to improve disease treatment approaches that are aimed to restore metabolic homeostasis, enhancing insulin sensitivity, and promoting  $\beta$ -cell survival and ultimately paving the way for improved

management of T2DM.<sup>[1]</sup> The limited success of current treatment strategies underscores the importance of proactive screening and early intervention before microvascular complications become clinically evident. By shifting towards an integrated approach that incorporates predictive role of biomarkers and systemic therapies, treating physicians can expand their range of treatment options, and thus increasing the chances of retaining vision and preventing the ongoing destructive processes in other organs affected by diabetes.<sup>[2]</sup> Diabetic Retinopathy (DR) is emerging as the most prevalent diabetes related complication, affecting a significant portion of the global diabetic population. Current estimates showed that around 382 million people are affected by DR throughout the world, establishing it as a major cause of diminution of vision and blindness among economically active age group individuals. The incidence of DR is expected to rise, highlighting the urgent need for early detection strategies and predictive biomarkers to improve disease management.<sup>[3,4]</sup> The increasing rates of DR subjects highlights the critical need for early screening and predictive biomarkers, such as Monocyte to HDL Ratio (MHR), to identify high-risk individuals before significant retinal damage occurs. Also this allows for an immediate treatment, that further leads to improvement in clinical outcome and reducing the socioeconomic burden associated with diabetes related blindness.<sup>[5]</sup> DR was responsible for 1.07% of total blindness and contributed to 1.25% of cases of moderate to profound visual loss.<sup>[6]</sup>

The development of DR is multifactorial and its pathogenesis is complex, involving a combination of metabolic and inflammatory processes. A major driver of DR progression is chronic inflammation, which is commonly associated with disorders in glucose and lipid metabolism, as seen in diabetes. Understanding the inflammatory mechanisms involved in DR is essential for developing more effective preventive and therapeutic strategies.<sup>[7,8]</sup>

Monocytes are a type of white blood cells which originate from their progenitor in the bone marrow. Because of their central role in inflammation, monocytes are considered key inflammatory biomarkers, providing valuable information about the severity and progression of inflammatory diseases including diabetic retinopathy. Therefore, monitoring monocyte levels or their associated cytokine production could provide important insights into managing diabetic retinopathy and other inflammation-driven diseases.<sup>[9]</sup> We are conducting this study to evaluate the association of hematological inflammatory marker MHR with DR and its severity in patients with T2DM as well as potential utility of MHR as a simple, cost effective and non-invasive biomarker for early recognition of diabetic retinopathy.

## MATERIALS AND METHODS

**Study Design and Participants:** This is an observational, cross-sectional study conducted at an outdoor department of tertiary and teaching care centre. A total of 186 patients with diagnosed T2DM were included after obtaining informed consent.

**Inclusion Criteria:** Patients aged more than eighteen years with a diagnosis of T2DM for more than five years were included.

**Exclusion Criteria:** Patients with aged less than eighteen years, diagnosed as type 1 diabetes mellitus, with chronic illness and inflammatory disease, malignancy, renal impairment, liver dysfunction, patient on lipid-lowering therapy and any other illness affecting retina were excluded to minimize confounding factors.

**Clinical and Laboratory Evaluation:** All participants underwent detailed history taking, physical examination and laboratory tests. Blood samples were analyzed for fasting blood glucose, HbA1c, complete blood count including monocyte count and serum lipid profile. MHR was calculated by dividing the absolute monocyte count by the HDL concentration (mg/dl)

Ophthalmological examination Fundus Photography for detecting DR performed using Direct Ophthalmoscopy, Indirect Ophthalmoscopy (20D) and slit lamp Biomicroscopy (90Dlens). Fluorescein Angiography is used to assess vascular abnormalities and Optical Coherence Tomography for measuring macular thickness. These patients were categorized into Five Groups Group A no DR (n=93), Group B Mild NPDR (n=35), Group C Moderate NPDR (n=24), Group D Severe NPDR (n=16), Group E PDR(n=18).

**Statistical Analysis:** We analysed the data using the statistical package SPSS, IBM version 29.0. Continuous variables were tested for normality using the Kolmogorov-Smirnov test. We calculated the descriptive measures such as mean and standard deviation (SD) with 95% confidence limits for normally distributed data. As appropriate, we compared mean values using the student's t-independent test or one-way analysis of variance test. Categorical data were presented as frequency and percentage values. We used the Chi-square test to compare the frequency data across the categories. A bivariate logistic regression analysis was carried out to evaluate the significant variables that will predict the outcome. The odds ratios with 95% confidence limits were measured for the statistically significant variables. To determine the cut off value for the significant predictor, ROC analysis was performed and using the Yuden index criteria, the cut off value was determined for an optimum sensitivity and specificity level. A two-tailed probability of P<0.05 was considered statistically considerable for all the statistical tests.

## RESULTS AND DISCUSSION

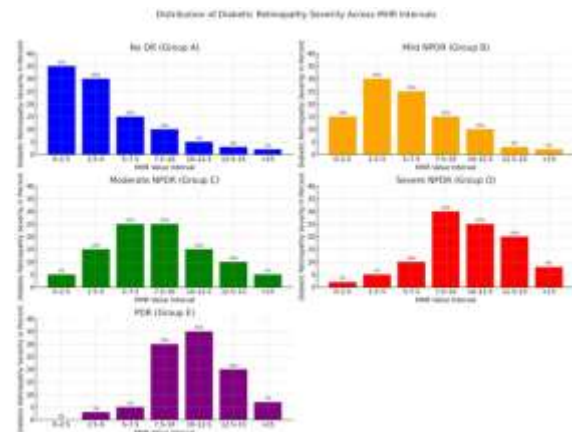
A total of 186 patients with diagnosed type 2 diabetes mellitus were included in the study. These patients were categorized into Five Groups Group A no DR (n=93), Group B Mild NPDR (n=35), Group C Moderate NPDR (n=24), Group D Severe NPDR (n=16), Group E PDR(n=18).

Figure 1 Illustrates the MHR values on X axis and percentage of patients without DR [Group A] and with DR [group B,C,D,E] on Y axis showed a progressive increase in MHR values with increasing DR severity when group analysis was done in between Group A and Group B,C,D,E. This is shown as patients without DR were largely concentrated in lower MHR categories (0 to 5), those with severe NPDR and PDR exhibited a shift towards higher MHR levels (7.5 to 15+), indicating a statistically and clinically relevant correlation between MHR and DR progression.

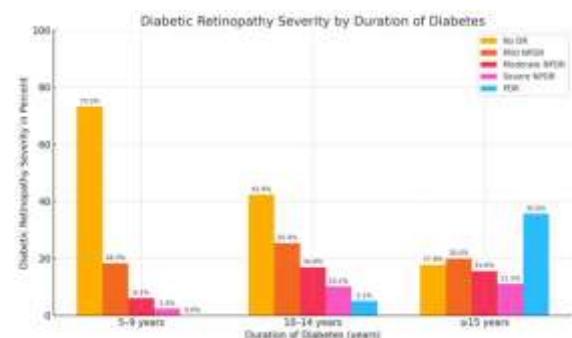
Figure 2 illustrates the distribution of diabetes duration on X axis 5 to 9 years, 10 to 14 years and more than 15 years and on Y axis diabetic retinopathy severity. A clear trend is observed wherein the proportion of patients without DR decreases with increasing diabetes duration, while the prevalence of more severe forms especially PDR increases. Notably, PDR was absent in the 5 to 9 year group but reached 35.6% in patients with diabetes for more than 15 years, indicating the strong association between longer diabetes duration and advanced DR stages.

The aim of this study was to investigate the potential role of MHR as a predictor of DR as well as its severity in individuals with T2DM. The objectives of our study were to determine the potential role of hematological inflammatory markers with a particular focus on the monocyte-to-HDL cholesterol ratio (MHR), in predicting DR among patients with T2DM. A total of 186 patients were evaluated on the basis of clinical, biochemical, and inflammatory parameters which were further compared between the retinopathy and no retinopathy groups to identify statistically significant association. Tang X et al. (2021) observed that inflammatory markers such as MHR, NLR, and PLR were elevated in T2DM patients, and these markers worsened with prolonged diabetes duration, reinforcing the current study's findings.<sup>[10,11]</sup> The degree of progression of DR increases with the duration of diabetes. These finding emphasizes the critical role of diabetes duration in the progression of DR, highlighting that each additional decade of hyperglycemia significantly increases the risk of developing severe forms of DR. Additionally, similar observations also seen by Deepika C Parameswarappa et al. (2021), where patients having T2DM for longer than 10 years exhibited more severe forms of DR, particularly proliferative forms, emphasizing the role of systemic inflammation in DR.<sup>[12,13]</sup> This study underscores the significant role

of MHR as an effective, non-invasive tool in predicting the severity of diabetic retinopathy in T2DM patients. There is also a strong correlation between elevated MHR and advanced stages of DR. These findings reinforce the results of previous studies such as that by Erdem B et al. (2022), which demonstrated a positive association between MHR and DR severity, particularly in patients with poor glycemic control and proliferative diabetic retinopathy.<sup>[14,15]</sup> This highlights the potential of MHR as a predictive biomarker for early detection and risk stratification in diabetic retinopathy.



**Figure 1: Correlation between Monocyte-to-HDL Ratio (MHR) and Percentage of patients with or without diabetic retinopathy (DR)**



**Figure 2: Comparison of Duration of Diabetes with Percentage of patients with or without diabetic retinopathy**

## CONCLUSION

This study establishes a significant correlation between the monocyte to high density lipoprotein ratio (MHR) and the severity of (diabetic retinopathy) DR in patients with T2DM. The data suggest that a positive correlation between MHR and increasing severity of DR, with the highest proportion seen in those with proliferative diabetic retinopathy (PDR). Importantly, these results support the concept that MHR reflects the underlying inflammatory mechanisms involved in the development and progression of diabetic retinopathy. Thus MHR remained an independent predictor of DR, even after adjusting for traditional risk factors such as keeping the blood glucose in

normal range and duration of diabetes. This suggests that systemic inflammation may play a critical role in the pathogenesis of diabetic retinopathy beyond metabolic derangements. Monocytes are key mediators of inflammation and vascular injury, whereas HDL exerts anti-inflammatory and protective vascular effects. So MHR acts as a composite biomarker that reflects the balance between proinflammatory and anti-inflammatory processes, that may contribute to retinal microvascular damage in diabetic patients.

Given that MHR is derived from routinely available laboratory parameters (complete blood count and lipid profile), it holds promise as a practical, inexpensive and easily accessible screening biomarker for DR that can be applied in routine clinical practice. This is particularly relevant for developing countries and resource limited settings with underserved remote areas where access to specialized ophthalmic care is limited. Implementing MHR screening in primary care settings could facilitate earlier identification of patients at risk for DR, enabling prompt referral for ophthalmologic evaluation and intervention. Moreover, it reinforces the inflammatory etiology of DR and highlights the importance of systemic inflammation in the pathogenesis and progression of diabetic retinopathy. In conclusion, MHR emerges as a promising, practical and non invasive biomarker associated with the presence and severity of diabetic retinopathy. It may serve as a adjunctive tool for risk stratification of DR among T2DM patients.

### Highlights

MHR is significantly associated with diabetic retinopathy severity in T2DM patients.

Higher MHR values correlate with advanced DR stages, particularly PDR.

MHR may be used as a cost-effective, non-invasive marker for screening of diabetic retinopathy.

### Limitations

While the present study provides valuable insight into the inflammatory basis of diabetic retinopathy and the potential role of hematological inflammatory ratios as predictive markers, there are several limitations as mentioned below.

The cross-sectional design does not allow for assessment of individual patient trajectories. Prospective data tracking MHR levels and DR changes over time would better validate the predictive value of MHR in the context of diabetes duration.

This study is conducted at a single institution, and the study population may not broadly reflect the variations in DR progression or MHR values seen in different demographic or geographic groups.

Authors contribution

K helped in concept, design; PN contributed to literature search; APK,NT,PG helped in data acquisition, data analysis, statistical analysis and

manuscript review; SK and CM contributed to manuscript preparation, manuscript editing

Financial support and sponsorship - None

Conflicts of interest: All authors have equally contributed in preparation of this manuscript and there is no conflict of interest.

**Ethical Aspects:**The study received Ethical approval from the Institutional Ethics Committee (SNMC/IEC/DHR/2025/109) Written informed consent was obtained from all participants prior to their inclusion in the study.

## REFERENCES

1. Hameed I, Masoodi SR, Mir SA, Nabi M, Ghazanfar K, Ganai BA. Type 2 diabetes mellitus: From a metabolic disorder to an inflammatory condition. *World J Diabetes*. 2015 May 15;6(4):598-612.
2. Sinclair SH, Schwartz SS. Diabetic retinopathy—an underdiagnosed and undertreated inflammatory, neuro-vascular complication of diabetes. *Frontiers in Endocrinology*. 2019 Dec 13;10:843:1-14.
3. Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes care*. 2012 Mar 1;35(3):556-64
4. Duh EJ, Sun JK, Stitt AW. Diabetic retinopathy: current understanding, mechanisms, and treatment strategies. *JCI insight*. 2017 Jul 20;2(14):e93751.
5. Zhang X, Saaddine JB, Chou CF, Cotch MF, Cheng YJ, Geiss LS, et al . Prevalence of diabetic retinopathy in the United States, 2005-2008. *Jama*. 2010 Aug 11;304(6):649-56.
6. Anjana RM, Deepa M, Pradeepa R, Mahanta J, Narain K, Das HK, et al. Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR-INDIAB population-based cross-sectional study. *The lancet Diabetes & endocrinology*. 2017 Aug 1;5(8):585-96.
7. Rani PK, Raman R, Sharma V, Mahuli SV, Tarigopala A, Sudhir RR, Kumaramanickavel G, Sharma T. Analysis of a comprehensive diabetic retinopathy screening model for rural and urban diabetics in developing countries. *British journal of ophthalmology*. 2007 Nov 1;91(11):1425-9.
8. Klein BE, Knudtson MD, Tsai MY, Klein R. The relation of markers of inflammation and endothelial dysfunction to the prevalence and progression of diabetic retinopathy: Wisconsin epidemiologic study of diabetic retinopathy. *Archives of ophthalmology*. 2009 Sep 14;127(9):1175-82.
9. Ganjali S, Gotto Jr AM, Ruscica M, Atkin SL, Butler AE, Banach M. Monocyte-to-HDL-cholesterol ratio as a prognostic marker in cardiovascular diseases. *Journal of cellular physiology*. 2018 Dec;233(12):9237-46.
10. Tang X, Tan Y, Yang Y, Li M, He X, Lu Y, et. al. Association of the Monocyte-to-High-Density Lipoprotein Cholesterol Ratio with Diabetic Retinopathy. *Frontiers in cardiovascular medicine*. 2021 Sep 21;8:707008.
11. Çallı Ü, Açıklan B, Demir G, Çoban F, Kocapınar Y. Association of monocyte to high-density lipoprotein cholesterol ratio with diabetic retinopathy in patients with type II diabetes mellitus. *Bosphorus Med J*. 2022;9(3):173-7.
12. Parameswarappa DC, Rajalakshmi R, Mohamed A, Kavya S, Munirathnam H, Manayath G, et. al. Severity of diabetic retinopathy and its relationship with age at onset of diabetes mellitus in India: A multicentric study. *Indian Journal of Ophthalmology*. 2021 Nov 1;69(11):3255-61
13. Jiang M, Yang J, Zou H, Li M, Sun W, Kong X. Monocyte-to-high-density lipoprotein-cholesterol ratio (MHR) and the risk of all-cause and cardiovascular mortality: a nationwide cohort study in the United States. *Lipids Health Dis*. 2022 Mar 18;21(1):30. doi: 10.1186/s12944-022-01638-6. PMID: 35300686; PMCID: PMC8931976.
14. Erdem, B., Kaya, Y. Prediction of diabetic retinopathy in patients with type 2 diabetes mellitus by using monocyte to high-density lipoprotein-cholesterol ratio. *Int J Diabetes Dev Ctries* 42.2022 oct ;741-746.
15. Solmaz I, Karahan M. Monocyte count/HDL cholesterol ratio: A new marker in diabetic retinopathy. *Annals of Medical of Research*. 2021 Feb 1;28(2).