Original Article

Monocyte to HDL Ratio (MHR) as an Early Predictor of Diabetic Retinopathy in Diabetes Mellitus

Pankaj Kumar Jain[1], Rajesh Yadav[2], Datar Singh[3], Sachin Kumar[3]

Abstract

Aims and Objective : To study Monocyte to HDL ratio (MHR) as an early predictor of Diabetic retinopathy in patients of Diabetes Mellitus.

Methodology : A total of 105 Diabetes Mellitus patients, 50 of whom had Diabetic retinopathy and 55 without diabetic retinopathy and 50 healthy controls were included in this cross-sectional study. Monocyte to HDL ratio was calculated by blood sampling after Fundus examination on all subjects.

Result : Monocyte to HDL ratio was higher in Diabetes Mellitus patients with Diabetic retinopathy compared to both the control group and without Diabetic retinopathy (p=0.00025). There was a significant positive correlation between Monocyte to HDL ratio and Diabetic retinopathy (r=0.26, p=0.001).

Conclusion : This study showed that patients with Diabetes Mellitus may be more likely to develop Diabetic retinopathy when they have high Monocyte to HDL ratio values. Based on this result Clinicians can also use Monocyte to HDL ratio as a new laboratory marker to predict Diabetic retinopathy at early stage.

Key words : Diabetes Mellitus, Diabetic Retinopathy, Monocyte to High Density Lipoprotein Ratio.

Diabetic Retinopathy (DR) constitutes a significant portion of visual impairments. It develops due to the destruction of capillaries, venules and arterioles in the retina caused by hyper-glycemia or insulin deficiency[1]. The prevalence of retinopathy is 35%[2]. The pathogenesis of Diabetic retinopathy is complex, with inflammation playing a crucial role in its development and progression, alongside factors such as hyper-glycemia and hypertension[3-6].

Diabetic retinopathy is one of the most significant diabetic microvascular complications and a leading cause of irreversible blindness among the working-age population Worldwide[7]. Various inflammatory cytokines and chemokines, such as ICAM-1, IL-1β, IL-6, IL-8, TNF-α, and MCP-1, have been found to be elevated in the serum, vitreous, and aqueous humour of diabetic patients with Diabetic retinopathy[8].

Monocytes releases proinflammatory cytokines at sites of inflammation, thereby influencing the severity of inflammation. This makes them an important inflammatory biomarker[9]. Additionally, plasma High-density Lipoprotein (HDL) cholesterol inversely correlates with DR risk[10,11] and has antioxidant properties that protect endothelial functions[12,13].

Editor's Comment :

- MHR serves as a simple and reliable indicator of systemic inflammation and is significantly associated with the presence and progression of Diabetic retinopathy.
- It may be utilized as an early predictor for Diabetic retinopathy in diabetic patients at resource limited settings.

The monocyte count to HDL ratio (MHR) can reflect the inflammatory status and is related to the development of diseases associated with chronic inflammation. MHR has been linked with the occurrence and prognosis of cardiovascular diseases, diabetic nephropathy and diabetic peripheral neuropathy[14-17]. In this context, the present study aims to investigate the associations between MHR and the prevalence of Diabetic retinopathy in adults with Diabetes Mellitus.

Materials and Methods

Study Population :

This cross-sectional study was conducted between 23/12/2023 to 23/06/24. A total of 105 patients, 50 of whom had Diabetic retinopathy, were included in the study. The control group consisted of 50 healthy individuals who are matched in terms of age and gender.

Department of General Medicine, Government Medical College, Kota, Rajasthan 324005
[1]MD, Professor
[2]MD, Resident and Corresponding Author
[3]MD, Resident
Received on : 13/12/2024
Accepted on : 27/04/2025

How to cite this article : Monocyte to HDL Ratio (MHR) as an Early Predictor of Diabetic Retinopathy in Diabetes Mellitus. Jain PK, Yadav R, Singh D, Kumar S. *J Indian Med Assoc* 2025; **123(11):** 54-7.

Participants who accepted to participate in the study were questioned in terms of age, gender, drug history, personal history like smoking, alcohol, past and family history.

Old ischemic disease, Old cerebrovascular accident, Haematological disease, Malignant disease and Autoimmune disease were excluded from the study.

Clinical Examination and Biochemical Analysis :

The diagnosis of DM was made according to the American Diabetes Association guidelines[18]. After fundoscopic examination was applied to all participants, the diagnosis of retinopathy was made. DR was diagnosed if any characteristic lesions existed as defined by the Early Treatment Diabetic Retinopathy Study (ETDRS). Peripheral venous blood samples were taken on OPD basis or within 24 hours of admission. Complete Blood Count including Monocyte count will be measured by an automated haematology analyser (Sysmex XS-800i, Japan) and manually corrected by pathologist to overcome by any technical error.

Routine biochemical test- Liver Function Test, Renal Function Test and Lipid Profile was performed by automated biochemistry analyser (Erba Mannheim EM-200 or Erba Mannheim XL-640).

Neutrophil/Lymphocyte Ratio (NLR), Monocyte/ Lymphocyte Ratio (MLR), Platelet/Lymphocyte Ratio (PLR) and MHR were calculated and recorded for each participant.

Statistical Analysis :

In all statistical analyses, SPSS 26.0 Statistical Package Program for Windows (SPSS Inc, Chicago, IL, USA) was used. The Kruskal-Wallis test, one-way ANOVA, and Fisher's exact test were used to compare the groups. The numeric variables as mean± SD and median (minimum-maximum) and the categorical variables as number and percent were expressed. Point biserial was applied to evaluate the correlation between the presence of DR and other parameters. Logistic regression analysis was used to calculate predictors of DR. MHR cut of value was calculated by Receiver Operating Characteristic (ROC) curve analysis to predict DR. A p-value of <0.05 was accepted as statistically significant.

Results

The study included 155 subjects, comprising 88 males (56.77%) and 67 females (43.22%). A statistical difference was observed among the three groups concerning gender, Total Leukocyte Count, Neutrophil Count, Platelet Count and HDL levels. Additionally, a statistical difference between groups 2 and 3 was noted in terms of insulin and statin use.

Statistically significance was found among all three groups for Haemoglobin, Lymphocyte count, Monocyte Count, HbA1C, Creatinine, Total Cholesterol, Triglyceride, NLR, MLR, PLR, and MHR (Table 1).

Positive correlations were identified between DR and HbA1C (r=0.49, p=0.001), monocyte count (r=0.2, p=0.014), Total Cholesterol (r=0.23, p=0.004) and MHR (r=0.26, p=0.001) (Table 2).

Regression analysis indicated that MHR is an

Table 1 — *Baseline characteristics and laboratory parameters of groups*

Parameter	Control (Group 1)	Without Dr (Group 2)	T2DM with Dr (Group 3)	P-Value
Age (Years)	49.7±19.29	53.76±14.82	56.64±12.5	0.09
Male n (%)	30 (60%)	28 (50.9%)	30 (60%)	0.55
Insulin n (%)	-	5 (9%)	6 (12%)	0.753
Statin n (%)	-	6 (10.90%)	9 (18%)	0.40
Hemoglobin (g/dl)	11.85 (5-16.2)	12.1 (6.6-17.6)	10.95 (6.3-16.1)	0.016
Tlc (10^3 µl)	9.07 (17-21)	8.1 (3.7-20.4)	7.5 (2.2-27)	0.804
Neutrophil (10^3 µl)	7 (0.8-20.530)	4.9 (1.8-20)	5.3 (1.1-24.12)	0.143
Lymphocyte (10^3 µl)	2.83 (0.63-8)	2.04 (0.27-4.6)	1.7 (0.30-3.93)	0.001
Monocyte (10^3 µl)	0.30 (0.09-0.73)	0.33 (0.09-1.37)	377.5 (0.08-1.6)	0.0016
Platelet (10^3 µl)	263 (23-625)	497 (390-536)	272 (180-587)	0.94
HbA1c (%)	5.7 (5-6.2)	8.2 (5.1-18.5)	10 (6-16.8)	0.00001
Creatinine (mg/dl)	1 (0.4-1.5)	0.9 (0.6-2.4)	1.1 (0.5-2.3)	0.00818
Cholesterol (mg/dl)	120.5 (61-240)	160 (65-292)	159.5 (59-371)	0.00004
Triglyceride (mg/dl)	95 (40-291)	142 (38-716)	148 (58-856)	0.00001
HDL (mg/dl)	46.5 (20-73)	40 (13-99)	40 (16-92)	0.1779
NLR	2.30 (0.5-3.44)	2.36 (0.54-74.07)	3.22 (1.09-22.33)	0.00023
MLR	0.12 (0.02-6.42)	0.14 (0.02-0.78)	0.21 (0.02-1.57)	0.0001
PLR	89.76 (18.37-586.25)	126.73 (10.42-518.75)	154.16 (0.11-660)	0.00015
MHR	6.18 (2.85-33)	8.46 (2.74-41.5)	11.01 (2.3-72.72)	0.00025

independent predictor of Diabetic retinopathy (Table 3).

ROC curve analysis for MHR showed that area under curve was 0.671 and p=0.004 Significance value (Fig 1).

Discussion

In the present study, differences in MHR were observed across all three groups. MHR was higher in patients with Diabetes Mellitus with DR compared to those without retinopathy and healthy controls. Additionally, MHR was found to be an independent predictor of DR.

Inflammation markers and monocytes play a crucial role in the development of diabetic complications[16]. Chronic retinal inflammation significantly contributes to the development of DR[7]. Monocyte levels increase in the retinal vessels, where they differentiate into macrophages that secrete inflammatory cytokines and growth factors, adhering to the outer surface of retinal capillaries. This leads to the breakdown of the blood-retinal barrier, increased retinal vascular permeability, and capillary non-perfusion, which are characteristic pathological features of early DR. Despite the known role of monocytes in DR development, studies have shown no direct relationship between blood monocyte count and DR[19]. Our study supports this evidence, finding that monocyte counts were significantly increased in patients with DR compared to healthy controls and patients without DR, aligning with previous findings. Hyper-glycemia enhances the inflammatory status, leading to the release of more neutrophils and monocytes from the bone marrow, which are then recruited into the retinal vessels, causing damage[20].

Table 2 — *Correlation of presence of diabetic retinopathy with other parameters*

Parameter	r	P
Age	0.14	0.079
Hemoglobin	-0.16	0.044
TLC	0.1	0.238
HbA1c	0.49	0.001
Neutrophil	0.06	0.472
Lymphocyte	-0.05	0.556
Monocyte	0.2	0.014
Platelet	0.01	0.928
Cholesterol	0.23	0.004
Triglyceride	0.1	0.199
HDL	-0.13	0.094
NLR	-0.07	0.41
MLR	-0.05	0.563
PLR	-0.03	0.722
MHR	0.26	0.001

Table 3 — *Univariate regression analyses to identify predictors of Diabetic retinopathy*

Parameter	Odd Ratio	95% C I	P
HbA1c	0.67	0.58-0.78	0.001
Monocyte	1	1-1	0.021
Cholesterol	0.99	0.98-1	0.006
MHR	1.07	1.02-1.12	0.004

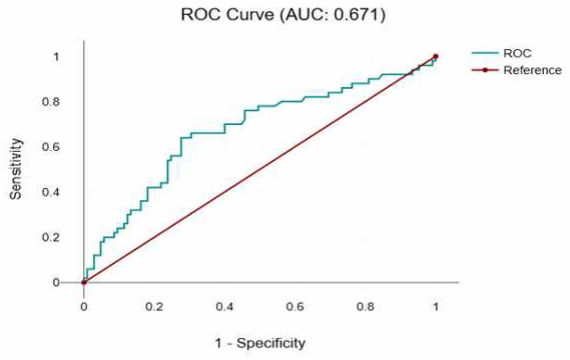

Fig 1 — *Receiver Operating Curve (ROC) analysis for MHR as a predictor of DR*

HDL transports cholesterol from peripheral tissues to the liver, prevents the harmful effects of LDL and reduces LDL oxidation. Furthermore, HDL inhibits monocyte activity, prevents monocytes from differentiating into macrophages, and limits the inflammatory response. It prevents endothelial dysfunction by removing cholesterol from lipid-loaded macrophages in atherosclerotic lesions. Lyons, *et al* study with 988 people showed that low HDL levels are a risk factor for DR[21]. Evidence indicates that poor control of triglycerides and LDL is associated with the incidence and progression of DR, while higher HDL levels and the use of lipid-lowering medication significantly reduce DR risk[22]. In our study, triglyceride levels were higher in the DR group compared to the other two groups, and HDL levels were higher in the control group compared to the other two groups. There was no difference in HDL levels between the T2DM with DR and without DR groups.

Considering the pro-inflammatory effects of the monocyte-macrophage system and the anti-inflammatory effects of HDL, combining these two parameters into a single inflammatory marker (MHR) is logical. Previous studies have shown that MHR is associated with many inflammatory diseases, particularly cardiovascular diseases. MHR has also been studied in DM and its complications, with high MHR linked to peripheral neuropathy, a common complication[14-17]. In our study, high MHR rates were observed in T2DM patients with DR, but not in those

without, suggesting that MHR can be used as a marker of inflammation and endothelial dysfunction for the development of DR. Recently, the ratios of these parameters (NLR, MLR, PLR, etc) have been defined as new inflammatory markers and are frequently studied in inflammation-related diseases[23]. Our study has shown that NLR, MLR, and PLR values are high in DR.

Moreover, compared to other expensive inflammatory markers, such as interleukin factors IL-1, IL-6, tumour necrosis factor-α, and monocyte chemo-attractant protein-1, the MHR can be easily calculated from a simple blood analysis, making this index more practical, cost-effective, and useful for predicting DR[8].

Conclusions

MHR was higher in patients with T2DM with DR compared to without retinopathy and healthy controls as well as there was positive correlation of MHR with DR. Also, MHR was determined to be an independent predictor of DR.

Based on these results, MHR could be an early predictor biomarker for DR.

Funding : None

Conflict of Interest : None

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