RESEARCH PAPER

Association of the Monocyte-to-High-Density Lipoprotein Cholesterol Ratio with Diabetic Retinopathy and Neuropathy in Adults with Type 2 Diabetes Mellitus: A Cross-Sectional Study

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Abstract

Background

Chronic low-grade inflammation and endothelial dysfunction contribute substantially to the development of diabetic microvascular complications. The monocyte-to-high-density lipoprotein cholesterol ratio (MHR) is an inexpensive composite inflammatory marker incorporating a pro-inflammatory cellular component and an anti-inflammatory lipid component. Emerging evidence suggests an association between elevated MHR and individual diabetic vascular complications; however, evidence regarding its relationship with multiple microvascular complications within the same type 2 diabetes mellitus (T2DM) population remains limited.

Objectives

To evaluate the association between MHR and diabetic retinopathy, neuropathy, and kidney disease risk among adults with T2DM.

Methods

Over the course of a year, 100 persons with type 2 diabetes who used the inpatient and outpatient services of a tertiary care hospital participated in this cross-sectional observational study. Demographic and clinical data were collected, and fasting laboratory investigations included absolute monocyte count, high-density lipoprotein cholesterol (HDL-C), glycated hemoglobin (HbA1c), serum creatinine, and urine albumin-to-creatinine ratio (ACR). MHR was computed by dividing the concentration of HDL-C by the absolute monocyte count. Diabetic retinopathy was assessed by fundoscopy, neuropathy by clinical neurological examination, and renal involvement was categorized according to Kidney Disease: Improving Global Outcomes (KDIGO) criteria using ACR and estimated glomerular filtration rate (eGFR) calculated by the CKD-EPI equation. Means and standard deviations were used to provide a summary of continuous variables and the relationship between MHR and microvascular complications were evaluated through the use of the right comparative tests.

Results

Half of the research participants were men, with a mean age of 57.96 +/- 13.71 years**.** The mean BMI was 26.39 ± 4.56 kg/m² and mean HbA1c was 7.12 ± 0.62%. Mean monocyte count, HDL-C, and MHR were 401.28 ± 49.88,

47.27 ± 8.30 mg/dL, and 8.92 ± 2.65, respectively. 38% of patients had retinopathy, with 13% having proliferative diabetic retinopathy and 25% having non-proliferative diabetic retinopathy. Neuropathy was clinically detected in 35% of participants.

MHR differed significantly according to retinopathy status. Mean MHR was 7.39 ± 1.31 among participants with normal fundoscopy, 10.36 ± 1.88 among those with non-proliferative diabetic retinopathy, and 13.41 ± 2.00 among those with proliferative diabetic retinopathy ($p < 0.01$). Participants with clinically detected neuropathy had significantly higher MHR than those without neuropathy (11.46 ± 2.33 vs. 7.55 ± 1.61; $p < 0.001$). In contrast, MHR was not significantly different between participants categorized as having moderately increased versus low kidney disease risk according to KDIGO criteria (8.94 ± 2.68 vs. 7.94 ± 0.42; $p = 0.083$).

Conclusions

Higher MHR was significantly associated with diabetic retinopathy and clinically detected diabetic neuropathy in this cohort of adults with T2DM. The association with KDIGO-defined kidney disease risk did not reach statistical significance. MHR may therefore represent a readily available inflammatory marker associated with selected diabetic microvascular complications. Larger prospective studies with standardized neuropathy assessment and longitudinal follow-up are required to determine whether MHR provides incremental prognostic information beyond established risk factors.

Keywords: type 2 diabetes mellitus; monocyte-to-HDL ratio; MHR; diabetic retinopathy; diabetic neuropathy; diabetic nephropathy; inflammation; microvascular complications

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Introduction

T2DM is a significant long-term metabolic condition which is linked to progressive micro and macrovascular complications. The causes of disability, poor quality of life, and early morbidity are diabetic retinopathy, neuropathy, and kidney disease. These complications develop as a multifactorial process that includes long-term hyperglycemia, oxidative stress, and endothelial dysfunction, dyslipidemia, and chronic low-grade inflammation.

There is growing recognition of inflammation as a key agent of diabetic vascular injury. Endothelial activation and tissue inflammation are caused by circulating monocytes migrating into injured vascular tissue and releasing pro-inflammatory mediators. Conversely, HDL-C, or high-density lipoprotein cholesterol, has anti-inflammatory, antioxidant, and endothelial-protective properties. Thus, the monocyte-to-HDL ratio of cholesterol (MHR) combines two physiologically opposing components and has been shown to be a useful proxy for oxidative stress and systemic inflammation.

Previous studies have demonstrated associations between elevated MHR and diabetic nephropathy, diabetic polyneuropathy, diabetic retinopathy, arterial stiffness, carotid atherosclerosis, and other vascular outcomes. Research papers used in the current thesis have also found increased MHR in diabetic nephropathy and diabetic polyneuropathy and also an independent relationship between MHR and diabetic retinopathy.

In spite of these observations, there is comparatively scanty data that has been used to assess the association between MHR and various microvascular manifestations in the same T2DM cohort. Notably, it is not yet clear whether MHR exhibits a uniform relationship between retinal, neurological, and renal manifestations.

Therefore, the present study evaluated the association between MHR and diabetic retinopathy, clinically detected neuropathy, and kidney disease risk among adults with T2DM.

Materials and Methods

Study design and setting

This 12-month cross-sectional observational study was carried out in the Department of General Medicine of tertiary care hospital in India. Adults with T2DM

presenting to the inpatient or outpatient services were screened for eligibility,100 were included in the study.

Participants

Adults with T2DM who were at least eighteen years old were eligible to participate. Patients with acute or chronic infections, hematological malignancies, autoimmune disease, corticosteroid therapy, chronic kidney disease, chronic liver disease, peripheral arterial disease, type 1 diabetes mellitus, gestational diabetes mellitus, pregnancy, or inability/unwillingness to participate were excluded.

All subjects provided written informed permission, and the research was carried out after receiving institutional ethics clearance.

Clinical and laboratory assessment

Demographic characteristics, anthropometric measurements, clinical history, and relevant medical-record information were collected.

Fasting venous blood samples were obtained for measurement of absolute monocyte count, HDL-C, fasting glucose, HbA1c, lipid parameters, and serum creatinine. Urine ACR was measured for assessment of albuminuria.

MHR was calculated as:

MHR = absolute monocyte count / HDL-C concentration

Assessment of microvascular complications

Diabetic retinopathy

Retinopathy was assessed by fundoscopy and categorized as normal, non-proliferative diabetic retinopathy (NPDR), or proliferative diabetic retinopathy (PDR).

Out of 100 participants, 62% had normal fundoscopy, 25% had NPDR, and 13% had PDR, with an overall prevalence of 38% retinopathy.

Diabetic neuropathy

Clinical neurological examination was used to measure neuropathy. Thirty-five percent (35) were diagnosed with neuropathy and 65% had no clinical neuropathy.

Kidney disease risk

The risk of kidney disease was classified based on KDIGO criteria in terms of urine ACR and eGFR calculated with CKD-EPI equation. There was a high level of albuminuria-related kidney disease prevalence among the study population with 98 percent showing moderately increased risk and 2 percent showing low risk.

Statistical analysis

The mean ± standard deviation was used to summarize continuous variables. Frequencies and percentages were used to summarize categorical variables. According to the original research, comparisons of MHR across groups with microvascular complications were carried out using the proper parametric tests. Statistical significance was defined as a two-sided p value of less than 0.05.

Associations were viewed as connections rather than temporal or causal effects due to the cross-sectional methodology.

Results

Baseline characteristics

A total of 100 participants were included. The mean age was 57.96 ± 13.71 years. Males constituted 51% and females 49% of the cohort. The largest age groups were 51–60 years (32%) and 61–70 years (27%). Seventy-one percent of participants belonged to the middle socioeconomic category.

The mean BMI was 26.39 ± 4.56 kg/m². Mean HbA1c was 7.12 ± 0.62%. The MHR ranged from 4.86 to 16.00, with a mean of 8.92 ± 2.65. Mean ACR was 60.22 ± 24.40, while mean serum creatinine and eGFR were 0.66 ± 0.14 and 104.53 ± 15.49, respectively.(Table 1)

Table 1. Baseline characteristics of the study population (n = 100)

Characteristic	Value
Age (years), mean ± SD	57.96 ± 13.71

Sex, male / female	51% / 49%
Age group 51–60 years	32%
Age group 61–70 years	27%
Middle socioeconomic category	71%
BMI (kg/m²), mean ± SD	26.39 ± 4.56
HbA1c (%), mean ± SD	7.12 ± 0.62
Absolute monocyte count, mean ± SD	401.28 ± 49.88 *(unit to be supplied)*
HDL-C (mg/dL), mean ± SD	47.27 ± 8.30
MHR, mean ± SD	8.92 ± 2.65
MHR, range	4.86–16.00
Urine ACR, mean ± SD	60.22 ± 24.40
Serum creatinine, mean ± SD	0.66 ± 0.14
eGFR, mean ± SD	104.53 ± 15.49

Retinopathy

Retinopathy was present in 38% of participants, with NPDR accounting for 25% and PDR for 13%.

A marked gradient in MHR was observed across retinal disease categories. Participants with normal fundoscopy had a mean MHR of 7.39 ± 1.31, compared with 10.36 ± 1.88 among those with NPDR and 13.41 ± 2.00 among those with PDR. The difference was statistically significant ($p < 0.01$).(Table2)

The progressively higher MHR across normal, NPDR, and PDR groups is notable and provides the strongest signal in the present study. However, because the study is cross-sectional, this gradient should be interpreted as an association rather than evidence that increasing MHR causes progression of retinopathy.(Figure1)

Figure 1. Mean MHR across retinopathy categories

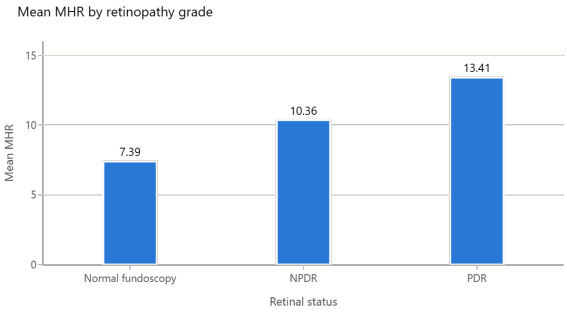


Table 2. Mean MHR according to retinopathy status

Retinal status	n (%)	Mean MHR ± SD
Normal fundoscopy	62 (62%)	7.39 ± 1.31
Non-proliferative diabetic retinopathy	25 (25%)	10.36 ± 1.88
Proliferative diabetic retinopathy	13 (13%)	13.41 ± 2.00
P		< 0.01

Neuropathy

Clinically detected neuropathy was present in 35% of participants.

Participants with neuropathy had substantially higher MHR than those without neuropathy (11.46 ± 2.33 vs. 7.55 ± 1.61). This difference was statistically significant ($t = 8.87$; $p < 0.001$).(Figure2,Table3)

Figure 2. Mean MHR in participants with and without clinically detected neuropathy

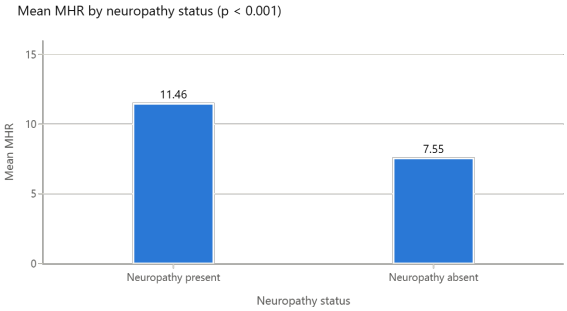


Table 3. Mean MHR according to neuropathy status

Neuropathy status	Frequency	Mean MHR ± SD
Clinically detected neuropathy	35% (n = 35)	11.46 ± 2.33
No clinical neuropathy	65%	7.55 ± 1.61
T		8.87
P		< 0.001

Kidney disease risk

The majority of participants were categorized as having moderately increased kidney disease risk according to KDIGO criteria. Mean MHR was 8.94 ± 2.68 in this group and 7.94 ± 0.42 among participants categorized as low risk. The difference was not statistically significant ($p = 0.083$).(Figure 3,Table 4)

Figure 3. Mean MHR by KDIGO kidney disease risk category

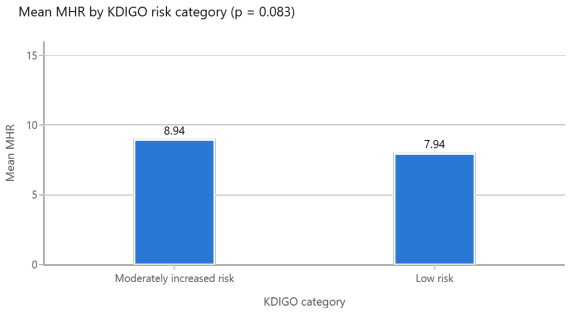


Table 4. Mean MHR according to KDIGO kidney disease risk category

KDIGO risk category	Frequency	Mean MHR ± SD
Moderately increased risk	98%	8.94 ± 2.68
Low risk	2%	7.94 ± 0.42
P		0.083

Therefore, the current investigation did not show a statistically significant correlation between MHR and KDIGO-defined kidney risk, in contrast to retinopathy and neuropathy.

Discussion

The principal finding of this study was that higher MHR was significantly associated with two clinically important diabetic microvascular complications—retinopathy and neuropathy. In contrast, no statistically significant association was demonstrated between MHR and KDIGO-defined kidney disease risk.

The association with diabetic retinopathy was particularly striking. Mean MHR increased from 7.39 in participants with normal fundoscopy to 10.36 among those with NPDR and 13.41 among those with PDR. This stepwise pattern suggests a relationship between higher systemic inflammatory burden, as reflected by MHR, and the presence of retinal microvascular disease.

These findings are biologically plausible. Diabetes-related hyperglycemia promotes oxidative stress, endothelial dysfunction, leukocyte activation, and inflammatory signaling. Monocytes may contribute to vascular injury through endothelial adhesion and release of inflammatory mediators, while impaired HDL-mediated antioxidant and endothelial-protective activity may further amplify vascular dysfunction. MHR is a potential measure of these conflicting processes under one routinely available laboratory index.

The current results are in line with the past studies used in the thesis. Tang et al. have found significantly increased MHR in patients with diabetic retinopathy and have proved that there is an independent relation between MHR and prevalence of retinopathy. Likewise, Çallı et al. found that patients with diabetic retinopathy had higher MHR and they found that there was a discriminatory cutoff in their sample.

The correlation of MHR with neuropathy was also significant. The mean MHR of the participants with clinically identified neuropathy was 11.46 and 7.55 in those without neuropathy. This finding agrees with previous literature demonstrating higher MHR in diabetic polyneuropathy and an inverse relationship between MHR and electrophysiological measures of nerve function.

Inflammation can also have a role in diabetic peripheral nerve injury by causing endothelial dysfunction, oxidative stress, impaired microvascular perfusion, and activation of inflammation. The means of neuropathy evaluation in the current study however, plays a significant role in the interpretation of this outcome. The diagnosis of neuropathy was done by clinical neurological examination as opposed to nerve conduction studies or quantitative neuropathy scores that have been validated. This means that mild or subclinical neuropathy could have been overlooked.

The renal results were varied. Mean MHR was numerically greater in those who were categorized as having moderately increased risk of kidney disease but this difference was not statistically significant (p = 0.083). The significance of this finding is that it averts overgeneralization of the observed association to all microvascular complications.

Positive correlations between MHR and albuminuria or diabetic nephropathy have been reported in the previous researches. Patients with diabetic nephropathy had higher MHR, and there was a positive association between MHR and the urine albumin-to-creatinine ratio, according to Karatas et al. The thesis also quotes prospective observational data that proved that there is a relationship between MHR and proteinuria.

Several explanations may account for the difference between those studies and the present findings. First, only two participants in the current cohort were classified in the low-risk KDIGO category, resulting in a markedly imbalanced comparison. Such imbalance substantially limits statistical power to detect differences between renal-risk groups. Second, the present study was cross-sectional and relatively small. Third, renal involvement was evaluated using a KDIGO risk categorization rather than longitudinal change in albuminuria or eGFR.

The study population itself provides useful clinical context. The cohort had a mean HbA1c of 7.12%, a mean BMI of 26.39 kg/m², and a relatively high burden of microvascular disease. Retinopathy was present in 38% and clinically detected neuropathy in 35% of participants.

The findings therefore support the concept that MHR may reflect an inflammatory phenotype associated with selected diabetic microvascular complications. Importantly, MHR is inexpensive and can be derived from routinely available complete blood count and lipid-profile measurements. This renders it possibly appealing to risk stratification of resources in clinical environments with limited resources.

However, MHR cannot be used as a substitute to current screening procedures at the moment. Fundoscopic retinal examination, correct evaluation of neuropathy, urine albumin examination and eGFR are vital parts of diabetic complication screening. Instead, MHR might be used as an adjunctive marker that can be used to determine people who might need further assessment.

Future research should establish whether MHR provides an additional predictive value to the already known clinical factors like diabetes duration, HbA1c, blood pressure, obesity, lipid parameters, and renal function. Future studies of larger sample sizes, standardized ophthalmological grading, verified neuropathy scores or nerve conduction studies, repeated MHR measures, and multivariate modelling would be especially helpful.

Strengths

To begin with, retinopathy, neuropathy and renal parameters were measured in the same T2DM cohort, which enabled comparison of the association between MHR and various microvascular phenotypes. Second, MHR is founded on laboratory parameters that are regularly available and, consequently, could have clinical feasibility. Thirdly, retinopathy was classified into NPDR and PDR, whereby the observed MHR gradient was evaluated in retinal disease categories.

Limitations

There was no evaluation of neuropathy with an electrophysiological measurement. The study is mindful of the fact that this methodology might be underestimating subclinical or asymptomatic neuropathy.

The renal-risk comparison appeared to be extremely skewed as per KDIGO criteria used for study, as 98% of the participants were found to have moderately increased risk, and only 2% of the participants were found to be of low risk. This reduces the possibility of making conclusive results about the connection between MHR and kidney disease using KDIGO.

Finally, longitudinal measurements of MHR were not available. Consequently, the study cannot determine whether changes in MHR precede, accompany, or follow development or progression of microvascular complications.

Conclusion

In this cross-sectional cohort of adults with T2DM, higher monocyte-to-HDL cholesterol ratio was significantly associated with diabetic retinopathy and clinically detected diabetic neuropathy. A marked increase in MHR was observed across normal fundoscopy, NPDR, and PDR categories, while patients with neuropathy also demonstrated substantially higher MHR than those without neuropathy. In contrast, the association between MHR and KDIGO-defined kidney disease risk was not statistically significant.

These findings support MHR as a potentially useful, inexpensive adjunctive inflammatory marker for identifying T2DM patients with selected microvascular complications. However, MHR should not be interpreted as an established predictive or diagnostic test on the basis of the present cross-sectional data. Prospective, multicenter studies with larger cohorts, standardized assessment of microvascular complications, and multivariable analysis are required to establish its independent prognostic value and determine whether incorporating MHR into routine diabetic risk assessment improves clinical outcomes.

Declarations

Ethics Approval and Consent to Participate: This study was conducted in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Institutional Ethics Committee.Written informed consent was obtained from all participants in their vernacular language prior to enrolment.

Consent for Publication: Not applicable. This manuscript does not contain any individual person's data in any form (images,videos, or voice recordings).

Availability of Data and Materials: The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request, subject to institutional requirements.

Competing Interests: The authors declare that they have no competing interests.

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