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A cross-sectional comparative study of the monocyte to high-density lipoprotein cholesterol ratio in normal individuals, type 2 diabetes mellitus, and diabetic nephropathy.

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Abstract

Background
Chronic low-grade inflammation plays a pivotal role in the progression of diabetes mellitus and its complications, particularly diabetic nephropathy. The Monocyte to HDL Cholesterol Ratio (MHR) has emerged as a novel inflammatory marker linked with cardiovascular and metabolic disorders. However, its clinical relevance across the spectrum of diabetes and nephropathy remains underexplored.
Objective: To compare the MHR among healthy individuals, patients with type 2 diabetes mellitus, and those with diabetic nephropathy, and to evaluate its correlation with renal function markers.

Methods
A cross-sectional comparative study was conducted among 100 participants divided into three groups: healthy controls (n = 30), diabetes mellitus without complications (n = 35), and diabetic nephropathy (n = 35). Monocyte count, HDL cholesterol levels, and renal function tests (serum creatinine, eGFR) were measured. MHR was calculated as the ratio of absolute monocyte count to HDL cholesterol. Statistical analysis was done using ANOVA and Pearson's correlation.

Results
The mean age of participants was 52.9 ± 7.7 years, with no statistically significant age difference among groups. Gender distribution was approximately balanced (55% male, 45% female).MHR values showed a progressive increase from healthy individuals (8.45 ± 1.56) to diabetic patients (13.27 ± 2.31), and were highest in diabetic nephropathy patients (18.65 ± 3.02) ($p < 0.001$). MHR was positively correlated with serum creatinine ($r = 0.52$, $p < 0.01$) and negatively with eGFR ($r = -0.47$, $p < 0.01$). Significant intergroup differences were observed across all parameters.

Conclusion
The study highlights that MHR significantly increases with disease progression from diabetes to diabetic nephropathy and correlates with declining renal function. MHR may serve as a simple, cost-effective inflammatory biomarker for early risk stratification in diabetic patients.

Recommendations
Routine inclusion of MHR in diabetic monitoring protocols may improve early detection of nephropathy and guide timely interventions in high-risk individuals.

***Keywords**: Monocyte to High-Density Lipoprotein Ratio, Diabetes Mellitus, Diabetic Nephropathy, Inflammation, High-Density Lipoprotein Cholesterol, Renal Function, Biomarker*
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Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. It is a global epidemic, with an estimated 537 million adults living with diabetes in 2021, and projections indicate this figure will rise to 643 million by 2030 (International

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Diabetes Federation, 2021). Diabetic nephropathy (DN), a common microvascular complication of diabetes, is the leading cause of end-stage renal disease (ESRD) worldwide, accounting for approximately 40% of ESRD cases. The timely identification of individuals at high risk for DN through reliable and affordable biomarkers is essential for preventing renal decline [1,2].

Chronic low-grade inflammation has emerged as a key mechanism in the development of insulin resistance, endothelial dysfunction, and microvascular injury, including nephropathy [2]. Traditional biomarkers such as serum creatinine and albuminuria have limitations in detecting early renal involvement. Consequently, hematological indices that reflect systemic inflammation are being investigated for their clinical utility. The Monocyte to High-Density Lipoprotein Cholesterol Ratio (MHR) has recently gained attention as a promising inflammatory marker, combining the atherogenic role of monocytes with the protective, anti-inflammatory function of HDL cholesterol [1,3].

Multiple studies have associated elevated MHR with adverse cardiovascular outcomes, metabolic syndrome, and inflammatory states in patients with type 2 diabetes mellitus (T2DM) [3,4]. MHR has also been linked to arterial stiffness and endothelial dysfunction—two important contributors to diabetic vascular complications—suggesting its role as a surrogate marker of vascular health in diabetics [4]. Moreover, elevated MHR levels have been observed in individuals with metabolic-associated fatty liver disease, further supporting its relevance in systemic metabolic inflammation [5].

While MHR has been evaluated in the context of diabetic retinopathy and vitamin D deficiency [1,6], few studies have specifically examined its role across the spectrum from healthy individuals to those with T2DM and established diabetic nephropathy [2,7]. A comparative assessment of MHR in these groups, along with its correlation to renal function markers such as estimated glomerular filtration rate (eGFR) and serum creatinine, may provide novel insights into its clinical applicability in early detection and risk stratification of diabetic nephropathy.

Therefore, this study aims to compare the MHR among normal healthy individuals, patients with type 2 diabetes mellitus, and those with diabetic nephropathy, and to investigate its correlation with renal function markers.

Materials and methods

Study design and setting

A hospital-based, cross-sectional comparative study was conducted in the Department of Biochemistry at Government Siddhartha Medical College (SMC), Vijayawada, Andhra Pradesh, India, from August 2023 to December 2024. SMC is a premier government medical institution affiliated with Dr. NTR University of Health Sciences. It is attached to a tertiary care teaching hospital that provides comprehensive inpatient and outpatient services to a diverse urban and semi-urban population. The institution encompasses a wide range of clinical specialties, making it a suitable center for conducting hospital-based biochemical and clinical research. The study aimed to evaluate and compare the Monocyte to High-Density Lipoprotein Cholesterol Ratio (MHR) among healthy individuals, patients with type 2 diabetes mellitus, and patients with diabetic nephropathy.

Study population and sample size

The study included a total of 100 participants, who were divided into three groups:

Group I: Healthy controls without diabetes (n = 30)

Group II: Patients diagnosed with type 2 diabetes mellitus without any microvascular complications (n = 35)

Group III: Patients diagnosed with diabetic nephropathy based on clinical and laboratory criteria (n = 35)

Participants were selected using purposive sampling from outpatient and inpatient departments of the institution.

Justification of study size

A total of 100 participants were chosen to allow for meaningful intergroup comparisons across three study categories, while ensuring feasibility within the study period. The sample size was based on similar published cross-sectional studies examining MHR in diabetic populations, which included group sizes ranging from 25 to 40 participants. This sample size was sufficient to achieve statistical power for detecting significant differences in MHR values between groups with an expected effect size and p-value < 0.05.

Inclusion criteria

- Age between 30 and 65 years
- For Group II and III: confirmed diagnosis of type 2 diabetes mellitus
- For Group III: presence of diabetic nephropathy (based on elevated serum creatinine, albuminuria, and reduced eGFR)

Exclusion criteria

- History of acute infections, chronic inflammatory diseases, malignancy, or autoimmune conditions
- Use of lipid-lowering or immunosuppressive medications

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- Pregnant or lactating women

Data collection procedure

After obtaining institutional ethical clearance and written informed consent, data were collected using a structured case record form. Demographic information and clinical history were recorded. Blood samples were collected after overnight fasting for the estimation of:

Monocyte count (from complete blood count)
High-Density Lipoprotein (HDL) cholesterol (using the enzymatic method)
Serum creatinine
The Estimated Glomerular Filtration Rate (eGFR) was calculated using the CKD-EPI formula.
MHR Calculation
MHR was calculated as the ratio of **absolute monocyte count (×10³/µL)** to **HDL cholesterol (mg/dL)**.

Bias and mitigation strategies

To minimize selection bias, purposive sampling was applied using clearly defined inclusion and exclusion criteria. Measurement bias was reduced by using standardized, calibrated equipment and validated laboratory methods for all biochemical analyses. To prevent observer bias, all sample analyses were conducted by technicians blinded to the group allocation. Furthermore, data entry was double-checked independently to ensure accuracy and reduce data processing errors.

Statistical analysis

Data were entered and analyzed using SPSS version 25.0. Descriptive statistics were expressed as mean ± standard deviation. Intergroup comparisons were performed using one-way ANOVA, followed by Tukey's post hoc test for pairwise comparisons. Correlation between MHR and renal parameters (serum creatinine, eGFR, and duration of diabetes) was analyzed using Pearson's correlation coefficient. A p-value < 0.05 was considered statistically significant.

Ethical considerations

The study was approved by the Institutional Ethics Committee of Siddhartha Medical College, Vijayawada (Approval No: IECSMCGGH/2023/AP/111). Written informed consent was obtained from all participants after explaining the study's purpose, procedures, and their right to withdraw at any time. Participant confidentiality and anonymity were maintained throughout. The data collected were used solely for research purposes. The study adhered to the ethical principles of the Declaration of Helsinki, ensuring respect, autonomy, and minimal risk to all participants.

Results

Participants

A total of 132 individuals were initially screened for eligibility to participate in the study. Of these, 18 were excluded due to not meeting the inclusion criteria (such as presence of acute infections, use of lipid-lowering or immunosuppressive medications, or autoimmune conditions), and 14 individuals declined to participate or did not provide informed consent. Consequently, 100 eligible participants were enrolled and classified into three study groups:

Group I (Healthy Controls): 30 participants
Group II (Type 2 Diabetes Mellitus without complications): 35 participants
Group III (Diabetic Nephropathy): 35 participants

The recruitment process and reasons for exclusion are depicted in Figure 1.

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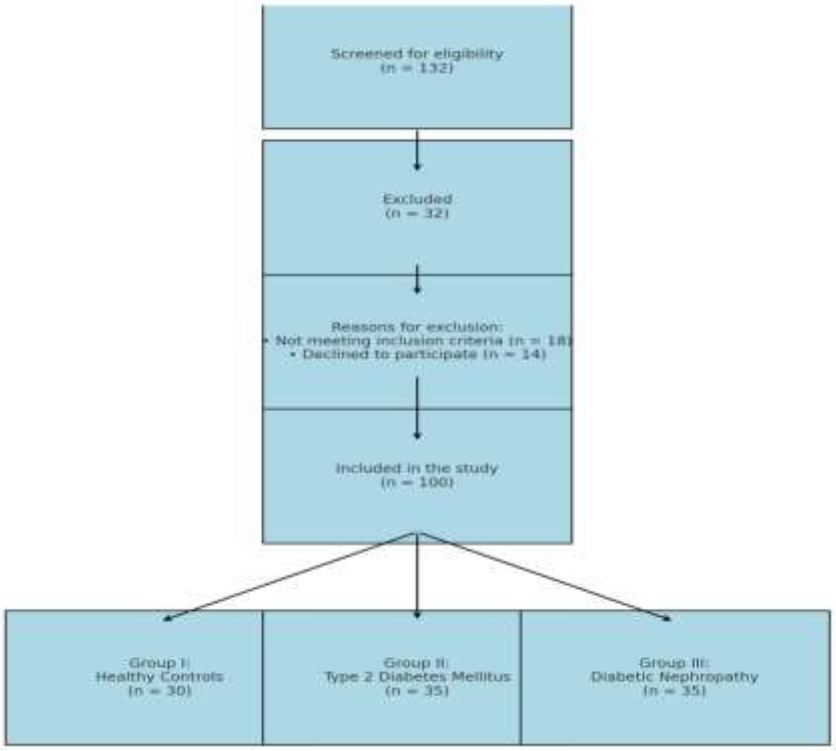

Figure 1. Participant flow diagram

The baseline demographic and clinical characteristics of the enrolled participants are summarized in Table 1. The mean age of participants was 50.3 ± 6.4 years in Group I, 53.9 ± 7.8 years in Group II, and 54.2 ± 8.2 years in Group III. The gender distribution was relatively balanced across the groups and showed no statistically significant difference ($p > 0.05$). Additionally, the duration of diabetes and body mass index (BMI) were significantly higher in the diabetic groups, particularly in those with nephropathy ($p < 0.05$).

Table 1: Demographic and Clinical Profile of Study Participants (n = 100)

Variable	Group I: Healthy Controls (n=30)	Group II: Type 2 DM (n=35)	Group III: Diabetic Nephropathy (n=35)	***p*-value**
Mean age (years)	50.3 ± 6.4	53.9 ± 7.8	54.2 ± 8.2	0.078
Gender (M/F)	16/14	19/16	20/15	0.912
Duration of diabetes (years)	N/A	6.2 ± 3.1	10.7 ± 4.5	<0.001
BMI (kg/m²)	23.8 ± 2.4	25.3 ± 2.8	26.1 ± 3.0	0.032

Data are presented as mean ± standard deviation; significance determined by one-way ANOVA or chi-square as appropriate.

Monocyte to HDL cholesterol ratio (MHR) among study groups

There was a statistically significant elevation in the Monocyte to HDL Cholesterol Ratio (MHR) across the three study groups. Group I (healthy controls) exhibited the lowest MHR values (8.45 ± 1.56), followed by Group II (13.27 ± 2.31), while Group III (diabetic nephropathy) demonstrated the highest values (18.65 ± 3.02). One-way ANOVA revealed a significant difference in MHR between the groups ($F = 108.42$, $p < 0.001$). Post hoc Tukey's HSD test confirmed that all intergroup differences were statistically significant ($p < 0.001$ for each pairwise comparison). These findings are summarized in **Table 2**.

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Table 2: Comparison of Monocyte Count, HDL Cholesterol, and MHR Among Groups

Parameter	Group I: Healthy Controls	Group II: Type 2 DM	Group III: Diabetic Nephropathy	*p*-value
Monocyte count ($\times 10^3/\mu L$)	0.49 ± 0.07	0.61 ± 0.09	0.75 ± 0.10	<0.001
HDL cholesterol (mg/dL)	58.1 ± 4.3	46.0 ± 3.8	40.2 ± 4.0	<0.001
MHR (Monocyte/HDL ratio)	8.45 ± 1.56	13.27 ± 2.31	18.65 ± 3.02	<0.001

All values are expressed as mean ± SD. Significance was tested using one-way ANOVA and Tukey's post hoc test.

Groups

Additionally, monocyte counts progressively increased from Group I to Group III, whereas HDL cholesterol levels showed an inverse trend. This supports the hypothesis that systemic inflammation (as indicated by higher monocyte counts) and dyslipidemia (lower HDL) are more pronounced in diabetic complications, particularly nephropathy.

Correlation Between MHR and Renal Parameters

Pearson correlation analysis revealed that MHR was positively correlated with serum creatinine levels ($r = 0.52$, $p < 0.01$) and negatively correlated with estimated glomerular filtration rate (eGFR) ($r = -0.47$, $p < 0.01$), indicating that higher MHR is associated with declining renal function. These results underscore the potential utility of MHR as an early inflammatory biomarker in the progression of diabetic nephropathy. The correlation results are detailed in **Table 3**.

Table 3: Correlation of MHR with renal function indicators in diabetic population (n = 70)

Correlated Parameter	Pearson's ***r***	***p*-value**
MHR vs. Serum Creatinine	0.52	<0.01
MHR vs. eGFR	-0.47	<0.01
MHR vs. Duration of Diabetes	0.38	<0.05

Correlation is significant at the $p < 0.05$ level.

Discussion

This study evaluated the Monocyte to HDL Cholesterol Ratio (MHR) among healthy individuals, patients with type 2 diabetes mellitus (T2DM), and those with diabetic nephropathy (DN), and explored its relationship with renal function indicators. The results demonstrated a statistically significant and progressive increase in MHR from healthy controls to T2DM and further to DN, suggesting that MHR may be a reliable marker of systemic inflammation and disease progression in diabetic populations.

The mean MHR in healthy controls (8.45 ± 1.56) was substantially lower than in patients with T2DM (13.27 ± 2.31) and DN (18.65 ± 3.02), with $p < 0.001$. These findings are in agreement with prior studies that have demonstrated elevated MHR in patients with diabetes and its complications, including DN [8,9]. The underlying mechanisms likely involve chronic low-grade inflammation, a key contributor to insulin resistance, endothelial dysfunction, and microvascular injury, which are hallmarks of diabetic nephropathy.

Monocytes act as key effectors in inflammatory cascades, while HDL cholesterol exhibits anti-inflammatory and antioxidative functions. Therefore, an elevated MHR indicates a shift toward heightened systemic inflammation. This supports previous findings where increased MHR was associated with proteinuria and reduced renal function in T2DM and DN patients [9,10].

In this study, MHR showed a significant positive correlation with serum creatinine ($r = 0.52$, $p < 0.01$) and a negative correlation with estimated glomerular filtration rate (eGFR) ($r = -0.47$, $p < 0.01$). Similar trends have been observed in prior studies that investigated the role of MHR in diabetic kidney disease, where MHR levels paralleled the severity of albuminuria and renal impairment [8,10]. Additionally, the observed inverse association between HDL levels and renal dysfunction reinforces the evidence that nephropathy is often accompanied by declining HDL, attributed to reduced synthesis and increased catabolism in diabetes [8,11].

A significant positive correlation between MHR and duration of diabetes ($r = 0.38$, $p < 0.05$) was also identified. This aligns with findings from earlier research that longer duration of diabetes is associated with increased systemic

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inflammation and metabolic burden [10,12]. As diabetic complications often progress subclinically, elevated MHR may serve as a useful early biomarker for identifying patients at higher risk for nephropathy.

From a clinical perspective, MHR presents a valuable, inexpensive, and readily available marker derived from routine complete blood count and lipid profiles. Given its significant correlation with renal dysfunction and disease progression, incorporating MHR into regular diabetic evaluations may improve early detection and risk stratification, especially in resource-constrained settings where advanced renal biomarkers are less accessible [11,12].

Generalizability

The findings of this study provide valuable insights into the relationship between Monocyte to High-Density Lipoprotein Cholesterol Ratio (MHR) and the progression from type 2 diabetes mellitus to diabetic nephropathy. However, the generalizability of these results may be limited due to the single-center, hospital-based setting and the use of purposive sampling. Participants were recruited from a tertiary care government medical college, which may not fully represent the broader community, particularly rural or primary care populations. Despite these constraints, the consistency of our results with similar published studies enhances their external validity. Future multi-center studies with larger, more diverse populations are recommended to strengthen the applicability of MHR as a predictive biomarker in varied clinical settings.

Conclusion

This study highlights the significant elevation of the Monocyte to HDL Cholesterol Ratio (MHR) in patients with type 2 diabetes mellitus and diabetic nephropathy compared to healthy individuals. The progressive increase in MHR, along with its strong correlation with serum creatinine and inverse association with eGFR, underscores its potential as a simple, cost-effective inflammatory biomarker reflecting renal dysfunction and disease progression. Given its accessibility through routine blood tests, MHR may serve as a valuable tool for the early identification of diabetic complications. Incorporating MHR into regular diabetic evaluations may facilitate timely interventions and improve clinical outcomes, particularly in resource-limited healthcare settings.

Limitations

However, the study has some limitations. Being a cross-sectional design, it does not establish causality. Longitudinal studies are warranted to assess whether elevated MHR precedes or predicts the onset of diabetic nephropathy. Furthermore, other confounding variables such as dietary factors, smoking status, and medication use were not assessed in this study and could influence monocyte counts and HDL levels.

Recommendations

Based on the study findings, it is recommended that the Monocyte to HDL Cholesterol Ratio (MHR) be included as a routine inflammatory marker in the clinical assessment of patients with type 2 diabetes mellitus. Early identification of elevated MHR can help clinicians stratify patients at risk for diabetic nephropathy and initiate timely interventions. Further longitudinal studies are advised to validate MHR as a predictive biomarker for renal complications and to establish standardized cut-off values for clinical application.

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List of abbreviations

DM – Diabetes Mellitus
DN – Diabetic Nephropathy
MHR – Monocyte to HDL Cholesterol Ratio
HDL – High-Density Lipoprotein
T2DM – Type 2 Diabetes Mellitus
eGFR – Estimated Glomerular Filtration Rate
BMI – Body Mass Index
CBC – Complete Blood Count

Source of funding

The study had no funding.

Conflict of interest

The authors declare no conflict of interest.

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Author contributions

SYCB-Concept and design of the study, results interpretation, review of literature, and preparing the first draft of the manuscript. Statistical analysis and interpretation, revision of manuscript. MS-Concept and design of the study, results interpretation, review of literature, and preparing the first draft of the manuscript, revision of the manuscript.DTD-Review of literature and preparing the first draft of the manuscript. Statistical analysis and interpretation. MP-Concept and design of the study, results interpretation, review of literature, and preparing the first draft of the manuscript. Statistical analysis and interpretation, revision of manuscript.

Data availability

Data is available upon request.

Author biography

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