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Study on the Association of Monocyte Lymphocyte Ratio Proliferative Diabetic Retinopathy and Control of Diabetes

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HIGHLIGHTS

1. Monocyte-lymphocyte ratio linked to retinopathy.
2. Elevated ratio may indicate disease progression.
3. Helps assess control in diabetic patients.
4. Potential marker for retinal health monitoring.
5. Association crucial for managing diabetes complications.

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ABSTRACT

This cross-sectional study aimed to assess the clinical and predictive significance of the monocyte-to-lymphocyte ratio (MLR) in type 2 diabetes mellitus patients with proliferative diabetic retinopathy (PDR). The study was conducted on 100 diabetic retinopathy patients admitted to the General Medicine Department at Kempegowda Institute of Medical Sciences over an 18-month period. Fundoscopy was used to diagnose and classify diabetic retinopathy into non-proliferative (NPDR) and proliferative (PDR) forms. Blood investigations, including a complete blood count (CBC) and HbA1c, were performed, and statistical analyses were conducted using SPSS (Version 26.0). The results indicated that the mean age of the study participants was 66.89 ± 13.16 years, with 62% being male. Among the study group, 80% had NPDR, and 20% had PDR. The mean duration of diabetes mellitus was 9.90 ± 2.96 years, with a mean HbA1c level of 8.80 ± 1.11, reflecting suboptimal glycemic control. The mean MLR for the entire cohort was 0.176 ± 0.0791, with PDR patients exhibiting a lower MLR (0.162 ± 0.074) compared to NPDR patients (0.179 ± 0.080); however, this difference was not statistically significant ($p = 0.373$). No significant correlation was found between the MLR and HbA1c levels ($r = -0.071$; $p = 0.484$), suggesting that MLR does not have a meaningful relationship with glycemic control in this population. Additionally, ROC curve analysis revealed an AUC of 0.438, with high sensitivity (95%) and specificity (98.8%) but poor overall diagnostic utility for MLR in predicting PDR. The findings indicate that while MLR may have some relevance in diabetic retinopathy, its predictive ability for PDR is limited.

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INTRODUCTION

Diabetic retinopathy (DR) is a severe complication of diabetes mellitus and stands as one of the leading causes of blindness, especially among the working-age population. As the incidence of diabetes continues to rise globally, the number of individuals at risk for diabetic retinopathy also increases, making it a significant public health issue. This sight-threatening condition results from the long-term effects of diabetes on the microvasculature of the retina, leading to progressive vision loss if left untreated. The pathogenesis of diabetic retinopathy is complex and involves multiple mechanisms, including hyperglycemia-induced oxidative stress, advanced glycation end products, and chronic low-grade inflammation. Among these, the role of inflammation has garnered significant attention in recent years. This has prompted researchers to investigate inflammatory markers as potential contributors to the progression of diabetic retinopathy[1-2].

Inflammation plays a pivotal role in the pathophysiology of many chronic conditions, including diabetic retinopathy. The chronic hyperglycemic state in diabetes triggers a cascade of inflammatory responses, contributing to endothelial damage and vascular dysfunction, which are hallmark features of diabetic retinopathy. In this context, several studies have explored the involvement of white blood cell (WBC) count and its subtypes as indicators of systemic inflammation in diabetic patients. WBCs, particularly their subtypes such as neutrophils, lymphocytes, and monocytes, have been associated with the inflammatory process that underpins diabetic retinopathy[3-4].

Among the various inflammatory markers, the monocyte-lymphocyte ratio (MLR) has emerged as a novel and promising indicator of systemic inflammation. The MLR represents the ratio of circulating monocytes to lymphocytes in the peripheral blood and has been identified as a key marker in the prognosis and prediction of several inflammation-related diseases, including cardiovascular diseases, certain cancers, and diabetic retinopathy. Inflammatory markers like the MLR reflect the balance between pro-inflammatory and anti-inflammatory responses within the body, where monocytes typically promote inflammation, and lymphocytes help modulate the immune response[4-5].

Monocytes, which are part of the body's innate immune system, play a critical role in the inflammatory response by migrating to sites of tissue damage and differentiating into macrophages. Macrophages, in turn, release pro-inflammatory cytokines and reactive oxygen species, which further propagate the inflammatory response. On the other hand, lymphocytes, particularly T and B cells, are components of the adaptive immune system and help regulate the inflammatory process by producing anti-inflammatory cytokines and antibodies that neutralize pathogens or damaged cells. In diabetic retinopathy, an imbalance in the monocyte-lymphocyte ratio may signify an excessive inflammatory response, potentially leading to further retinal damage[4-6].

The monocyte-lymphocyte ratio has been shown to have clinical and prognostic value in a variety of conditions. In cardi--ovascular diseases, a high MLR has been associated with worse outcomes, indicating the ratio's ability to predict adverse events. Similarly, in cancer, MLR is used as a prognostic marker, with higher ratios correlating with poor survival rates. In the context of diabetes and diabetic retinopathy, the relationship between MLR and disease progression is an area of active investigation. Some studies have demonstrated that elevated MLR levels are associated with more advanced stages of diabetic retinopathy, particularly proliferative diabetic retinopathy (PDR), which is the most severe form of the disease. PDR is characterized by the growth of new, abnormal blood vessels on the retina, a process driven by chronic inflammation and hypoxia[5-7].

Given the potential significance of MLR in diabetic retinopathy, this study aims to explore the clinical and predictive value of the monocyte-lymphocyte ratio in patients with type 2 diabetes mellitus, particularly those with proliferative diabetic retinopathy. By investigating the relationship between MLR and the severity of diabetic retinopathy, this research seeks to provide further insights into the role of inflammation in the progression of the disease. Specifically, the study will evaluate whether MLR can be used as a reliable marker to predict the development and severity of proliferative diabetic retinopathy in patients with type 2 diabetes[4-7].

Understanding the relationship between MLR and diabetic retinopathy could have significant clinical implications. If MLR proves to be a reliable predictor of proliferative diabetic retinopathy, it could be used as a non-invasive, cost-effective marker for early identification of patients at high risk for developing severe retinal complications. This, in turn, could facilitate earlier intervention and more personalized treatment approaches, potentially preventing vision loss and improving the quality of life for patients with diabetes[7].

Moreover, by identifying inflammation as a key contributor to the progression of diabetic retinopathy, the study may pave the way for the development of new therapeutic strategies targeting the inflammatory pathways involved in the disease. For example, anti-inflammatory drugs or treatments that modulate the immune response could be explored as potential adjunctive therapies for patients with diabetic retinopathy, in addition to the standard treatments such as laser therapy and anti-vascular endothelial growth factor (VEGF) injections[8].

Diabetic retinopathy remains a major cause of blindness in the working population, and its pathogenesis is closely linked to inflammation. The monocyte-lymphocyte ratio, a novel inflammatory marker, may offer valuable insights into the development and progression of diabetic retinopathy, particularly proliferative diabetic retinopathy. This study aims to explore the clinical and predictive significance of MLR in patients with type 2 diabetes mellitus, potentially opening new avenues for early diagnosis and treatment strategies that could mitigate the devastating effects of this condition..

MATERIAL AND METHODS

This cross-sectional study was conducted on 100 patients diagnosed with diabetic retinopathy, who were admitted to the

General Medicine Department at Kempegowda Institute of Medical Sciences over an 18-month period. Ethical approval for the study was obtained from the Ethical Approval Committee of Kempegowda Institute of Medical Sciences. Patients were recruited into the study based on the inclusion criteria, which required a confirmed diagnosis of diabetic retinopathy.

DATA ANALYSIS

The collected data was organized and compiled using Microsoft Excel. Descriptive statistics were applied to summarize the data, and statistical analyses were performed using SPSS software (Version 26.0). A significance level of 5% ($\alpha = 0.05$) was used throughout the analysis. Qualitative variables were presented as frequencies and percentages, while quantitative variables were expressed as means with standard deviations. The student's t-test was employed to assess the association between numerical and categorical variables, and Pearson's correlation was used to examine the relationships between numerical variables.

RESULTS

Our study provides an overview of patient characteristics in a study or clinical setting, focusing on diabetes-related factors. The average age of the patients is 66.89 years with a standard deviation (SD) of ±13.16, indicating some variation in the age distribution. The gender distribution shows a higher proportion of males (62%) compared to females (38%). The mean duration of diabetes mellitus (DM) is 9.9 years (SD ±2.96), which suggests the patients have had the disease for a significant amount of time. The average body mass index (BMI) is 23.85 (SD ±1.80), placing most patients in the healthy to slightly overweight range. The fundus examination shows that 80% of the patients have non-proliferative diabetic retinopathy (NPDR), while 20% have proliferative diabetic retinopathy (PDR), indicating varying stages of retinal complications related to diabetes.

Table 1: Association of Fundus Findings with Age, HbA1c and MLR

	Fundus		P VALUE
	NPDR	PDR	
Age	67.50±13.328	64.45±12.505	0.357
HbA1c	8.487±1.0681	10.065±0.8725	0.000
MLR	0.17±0.08	0.16±0.0749	0.373

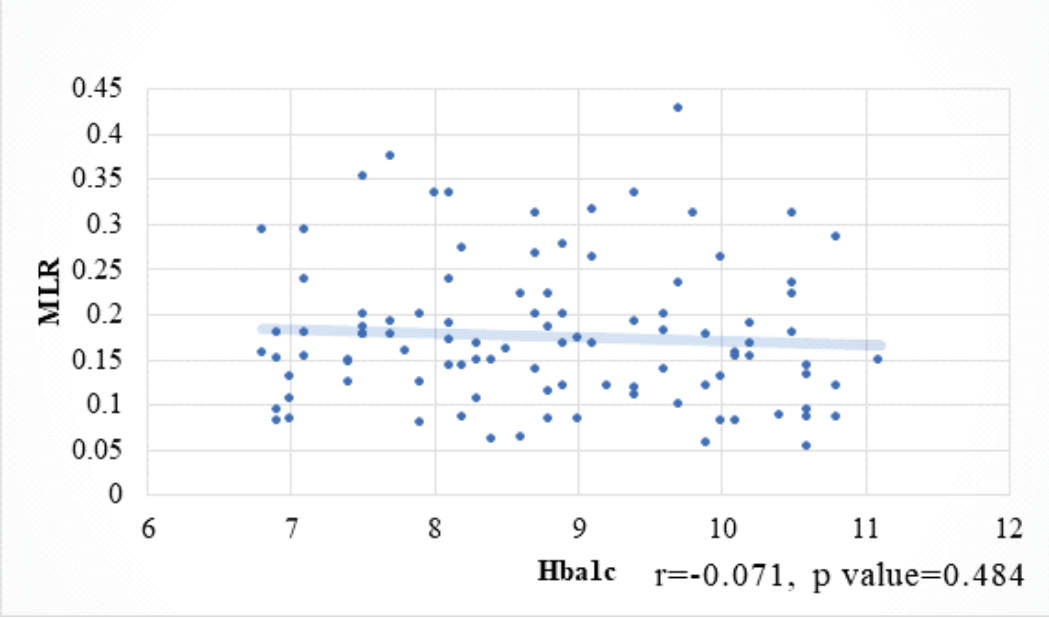

Figure 1: Correlation of MLR with HB1A1C

This table and scatter plot illustrate the association of age, HbA1c levels, and monocyte-lymphocyte ratio (MLR) with the severity of diabetic retinopathy, comparing patients with non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). The table shows no significant difference in age between NPDR and PDR groups ($p = 0.357$), indicating that age is not strongly associated with the progression to PDR. However, HbA1c levels are significantly higher in the PDR group (10.065) compared to the NPDR group (8.487), with a highly significant p value of 0.000, suggesting that poor glycemic control is strongly linked to more severe retinopathy. MLR, however, shows no significant association with retinopathy severity, as indicated by the p value of 0.373. The scatter plot further reinforces this, showing a weak and statistically insignificant correlation ($r = -0.071$, $p = 0.484$) between MLR and HbA1c levels, suggesting that MLR does not have a meaningful relationship with glycemic control in this population.

Table 3: ROC Analysis of MLR in Predicting PDR

Area Under the Curve - MLR				
Area	**S. E**	**P VALUE**	**95% CI**	
			Lower Bound	**Upper Bound**
0.438	0.071	0.396	0.300	0.577
CUT OFF		0.058		
Sensitivity		95%		
Specificity		98.8%		

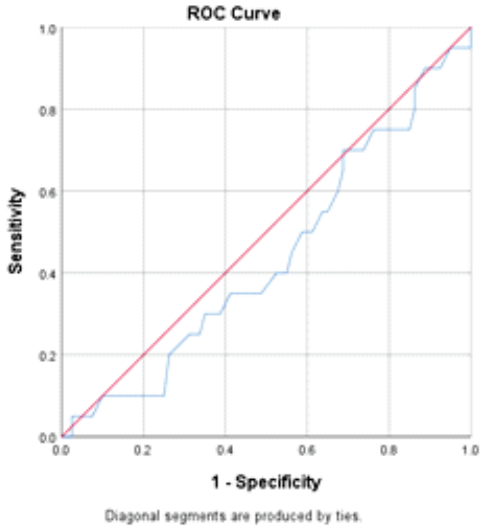

Figure 2

This table and ROC curve assess the diagnostic utility of the monocyte-to-lymphocyte ratio (MLR) in predicting a certain clinical outcome, with a focus on the Area Under the Curve (AUC). The AUC is 0.438, which is below 0.5, indicating that the MLR has poor discriminative ability for the condition being tested. The p-value of 0.396 suggests that the result is not statistically significant, reinforcing the lack of predictive power. The 95% confidence interval (CI) ranges from 0.300 to 0.577, further indicating wide uncertainty in the MLR's diagnostic value. Although the table shows a high sensitivity of 95% and specificity of 98.8%, these values are not reflected in the poor AUC and non-significant p-value, likely indicating that MLR is not a reliable diagnostic marker in this context. The ROC curve also visually shows that the MLR does not perform well, as the curve remains close to the diagonal line representing random chance.

DISCUSSION

Our study provides a comprehensive overview of patient characteristics in a clinical setting, focusing on diabetes-related factors, particularly those related to diabetic retinopathy. The average age of patients in our study was 66.89 years with a standard deviation (SD) of ±13.16, highlighting some variability in the age distribution. A higher proportion of males (62%) compared to females (38%) was observed, with the mean duration of diabetes mellitus (DM) being 9.9 years (SD ±2.96), indicating that the patients had lived with the disease for a considerable time. The average body mass index (BMI) of 23.85 (SD ±1.80) suggests that most patients fell within the healthy to slightly overweight range. Fundus examination revealed that 80% of patients had non-proliferative diabetic retinopathy (NPDR), while 20% were diagnosed with proliferative diabetic retinopathy (PDR), indicating a range of retinal complications among the study group. Similar findings were reported by Kalter Leibovici et al. (1997) and Jang HN et al. (2022) where the majority of patients with diabetic retinopathy were aged over 60 years and had BMI values placing them in the healthy to slightly overweight categories. These consistent results across multiple studies further emphasize the prevalence of diabetic retinopathy in older populations, as well as the association with body weight that is not excessively high. Both in our study and in these earlier reports, the findings suggest that even within a normal to slightly elevated BMI range, the risk of developing complications such as diabetic retinopathy remains significant, especially in older adults who have had diabetes for extended periods. This highlights the need for continued monitoring of these factors in clinical practice to mitigate the progression of re-

-tinopathy.

In our study, the scatter plot illustrates the association between age, HbA1c levels, and monocyte-lymphocyte ratio (MLR) with the severity of diabetic retinopathy, comparing patients with non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). The data reveals no significant difference in age between the NPDR and PDR groups ($p = 0.357$), indicating that age is not a strong factor in the progression to PDR. However, HbA1c levels were significantly higher in the PDR group (10.065) compared to the NPDR group (8.487), with a highly significant p value of 0.000. This suggests that poor glycemic control is closely linked to more severe retinopathy. In contrast, MLR does not show a significant association with retinopathy severity, as reflected by the p value of 0.373. The scatter plot further supports this finding, showing a weak and statistically insignificant correlation between MLR and HbA1c levels ($r = -0.071$, $p = 0.484$), indicating that MLR does not have a meaningful relationship with glycemic control in this patient population.

Similar to our study Strassheim et al. (2019) also reported that elevated levels of inflammatory mediators can trigger early and sustained chronic inflammation in the diabetic retina. This inflammation contributes to leukocyte activation, adhesion to the vascular endothelium, disruption of the blood-retinal barrier, increased vascular permeability, and eventually, the development of macular edema. Like in our study, they emphasized that peripheral blood markers, including white blood cell (WBC) counts and their subtypes, are easily accessible and can serve as classic markers of inflammation. While our study did not find a strong association between MLR and glycemic control, Strassheim et al. findings highlight the broader role of systemic inflammation in diabetic retinopathy pathogenesis. This underscores the complexity of inflammation's role and the need for further investigation into more specific markers that could better predict retinopathy severity and progression[11].

In our study, the ROC curve was used to assess the diagnostic utility of the monocyte-to-lymphocyte ratio (MLR) in predicting a specific clinical outcome, with a particular focus on the Area Under the Curve (AUC). The AUC value of 0.438, which is below 0.5, indicates that MLR has poor discriminative ability for the condition being examined. The p-value of 0.396 further suggests that the result is not statistically significant, reinforcing the conclusion that MLR lacks predictive power in this context. The 95% confidence interval (CI) ranges from 0.300 to 0.577, reflecting considerable uncertainty in MLR's diagnostic value. While the table reports high sensitivity (95%) and specificity (98.8%), these values do not align with the poor AUC and non-significant p-value, implying that MLR is not a reliable diagnostic marker for this condition. The ROC curve visually confirms this, as the curve remains near the diagonal line, representing random chance.

Similar to our findings, previous studies by Mertoglu et al. (2017), Chen et al. (2019), and Liu et al. (2019) also reported that inflammatory markers such as the platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), and neutrophil-to-lymphocyte ratio (NLR) are potential indicators for diabetes and its complications. These studies suggest that while these markers hold promise, their predictive utility may be limited. Furthermore, research by Hu et al. (2019), Yue et al. (2017), and Wang et al. (2020) has similarly examined the associations between PLR, NLR, and MLR with the progression of diabetic retinopathy (DR). Like our study, their findings suggest that these ratios may be linked to DR progression, but the strength and reliability of their predictive power vary. Collectively, these studies highlight the ongoing need to explore and refine the use of these inflammatory markers in the diagnosis and management of diabetes-related complications, particularly diabetic retinopathy (15-17).

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