VOLUME - 12, ISSUE - 06, JUNE - 2023 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

General Medicine

A NOVEL DIAGNOSTIC APPROACH: NEUTROPHIL LYMPHOCYTE RATIO AND SERUM FERRITIN IN TYPE 2 DIABETES PATIENTS WITH DIABETIC NEPHROPATHY

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ABSTRACT

Introduction- DM is a chronic metabolic disease characterized by elevated blood sugar levels (hyperglycemia) caused by impaired insulin production, cellular insulin resistance, or both. DM is a systemic disease having severe microvascular and macrovascular complications. Diabetic nephropathy (DN), diabetic retinopathy, and diabetic neuropathy are examples of microvascular complications whereas stroke, cardiovascular diseases (CVDs), and peripheral vascular diseases are examples of macrovascular complications. DN is a common micro-angiopathic complication in patients with diabetes. Inflammation plays a crucial role in the development and progression of DN, as many inflammatory cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), interleukin-8 (IL-18), and tumor necrosis factor α (TNF-) contribute in the pathogenesis of DN. An increase in neutrophil count is seen in thrombus forming and ischemic diseases. The Neutrophil-Lymphocyte ratio (NLR) in complete blood count is studied in many cardiac and non-cardiac diseases as inflammatory marker and is used to predict the prognosis. Serum ferritin concentration is usually increased in poorly controlled type 2 diabetic patients reflecting increased oxidative stress. **Objectives-** To study the Neutrophil Lymphocyte ratio (NLR) and serum ferritin in patients of type 2 diabetes. **Methods-** A cross-sectional study was conducted on 150 patients with T2DM in SRN hospital, affiliated to MLNMC, prayagraj. Blood samples were taken to estimate CBC, LFT, KFT, S. Electrolyte, HbA1C, FBS/PPBS, S. ferritin and urine for microalbumin. Data was collected, entered in MS Excel Spreadsheet & appropriate statistical package applied. **Results-** The median NLR of the type 2 DM patients was 2.10. Of total 150 diabetic patients 26 patients (17.3%) were having nephropathy based on urine microalbumin. Based on nephropathy in patients of T2DM, two groups (A and B) were made. Group A includes patients with nephropathy, while Group B includes patient without Nephropathy. The mean Hb, MCV, and ALC were lower in Group A (T2DM patients with nephropathy) patients. In contrast, TLC, Mean ANC and NLR were higher in Group A (T2DM patients with nephropathy) patients. NLR and haemoglobin show a significant difference between both groups A and B. The mean S. ferritin levels were higher in Group A (T2DM patients with nephropathy) patients, difference was significant between both groups. In the present study, NLR was negatively correlated with S. ferritin with r= - 0.092, and the correlation was insignificant. **Conclusion-** the results of our study showed that there was a significant relation between NLR, S. ferritin and DN. Therefore, NLR and S. Ferritin may be considered as a novel surrogate marker of DN in early stages.

KEYWORDS : Neutrophil Lymphocyte Ratio, Serum Ferritin, Diabetic Nephropathy, Type 2 Diabetes

INTRODUCTION

Diabetes mellitus is a systemic disease having several microvascular and macrovascular complications. In diabetic patient's nephropathy is a common micro-angiopathic complication. It is one of the most common causes of end-stage renal disease (ESRD).

DN is clinically manifested as increased albumin excretion ranging from microalbuminuria to macroalbuminuria and eventually ESRD. However, the degree of albuminuria is not necessarily linked to disease progression in patients with DN associated with either type 1 or type 2 diabetes mellitus (T2DM).

In type 1 diabetes, once frank DN develops, there is persistent proteinuria, and its progression toward ESRD could only be slowed but could not be stopped [1,2]. Due to this, there is a need of early predictors of DN by which we can predict the disease and can halt the progression of the disease.

Multiple studies have explored the association between systemic inflammation and vascular disease indicated that chronic inflammation promotes the development and acceleration of micro- and macro-angiopathic complications in patients with diabetes.

Total white blood cell (TWBC) count is a crude but sensitive indicator of inflammation which can be done easily in lab. NLR in complete blood count is studied in many cardiac and noncardiac diseases as an inflammatory marker and is used to predict the prognosis of diseases such as acute myocardial infarction (MI), stroke, and Heart failure [3,4].

Iron stores expressed as Serum Ferritin concentration, have been proposed to be a component of the insulin-resistance syndrome. Indeed, the concentration of circulating ferritin was significantly associated with centrally distributed body fatness as well as with several other measurements of obesity [5].

Serum concentrations of ferritin are usually increased in poorly controlled type 1 and type 2 diabetic subjects, and ferritin has been shown to predict HbA1c independently of glucose, probably reflecting increased oxidative stress [6].

The current DN diagnosis depends on albuminuria as biomarker [7]. However, its diagnostic value in early-stage DN is limited because renal injury commonly precedes urinary albumin excretion [8].

OBJECTIVES

To study NLR and Serum Ferritin in patients of T2DM, whether theses can be used as a surrogate marker of Diabetic Nephropathy.

MATERIALS AND METHODS

An observational cross-sectional study was done from July 2021 to June 2022 in patients of medicine OPD. All diagnosed T2DM patients were enrolled in this study.

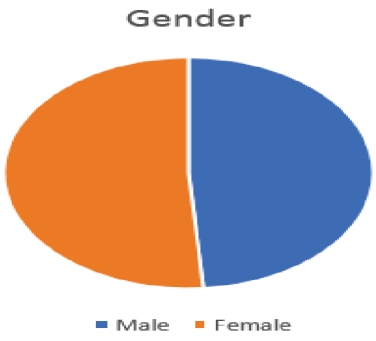
Patients with T1DM; patients with infections, chronic systemic diseases such as CVD, CKD, autoimmune disorder, malignancy; patients on anti-inflammatory drugs, steroids, ACR/ARBs, alcohol; patients having diseases affecting urinary protein excretion as nephrotic syndrome and patients having low glomerular filtration rate (GFR) without microalbuminuria were excluded from study.

Diagnosed T2DM patients were screened. Relevant history regarding Diabetes was collected. Complete physical examination was done.

CBC, LFT, KFT, ELECTROLYTE, FBS/PPBS, HbA1C, Lipid Profile, Serum ferritin, HBsAg, AntiHCV, HIV, Urine routine Microscopy, USG Abdomen, Urine Microalbumin, eGFR (method CKD- EPI creatinine equation 2021) was done for all patients.

RESULTS

This study comprised of 150 T2DM patients aged 22 to 78 years, with a mean age of 49.23±12.13 years; 48.7% of subjects were male, and 51.3% were female.



TLC, ANC and MCV were positively correlated with NLR while hemoglobin and ALC was negatively correlated. Hemoglobin, TLC, ANC and ALC were showing significant correlation with NLR.

Parameters	Spearman's rho Correlation coefficient	p value (on correlation with NLR)
Hb (gm/dl)	-0.200	0.014
TLC (cells/mm3)	0.326	<0.001
ANC (cells/mm3)	0.514	<0.001
ALC (cells/mm3)	-0.516	<0.001
MCV (fl)	0.107	0.191

TLC, ANC and ALC were positively correlated with S. Ferritin while Hemoglobin and MCV were negatively correlated. Hemoglobin was showing significant correlation with serum ferritin.

Parameters	Spearman's rho Correlation coefficient	p value (on correlation with S. Ferritin)
Hb (gm/dl)	-0.302	<0.001
TLC (cells/mm3)	0.049	0.550
ANC (cells/mm3)	0.044	0.596
ALC (cells/mm3)	0.019	0.814
MCV (fl)	-0.096	0.244

Urea, Creatinine and Urine microalbumin were positively correlated with NLR. Urea and Urine Microalbumin were significantly correlated with NLR. While eGFR was negatively correlated with NLR, and it was significant.

Parameters	Spearman's rho Correlation coefficient	p value (on correlation with NLR)
Urea (mg/dl)	0.206	0.012
Creatinine (mg/dl)	0.156	0.056
eGFR (ml/min/1.73m2)	-0.323	<0.001
Urine microalbumin (mg/dl)	0.163	0.047

Urea and eGFR were negatively correlated with S. Ferritin, but it was not significant. While creatinine and urine microalbumin were positively correlated with Serum ferritin, but it was also not significant.

Parameters	Spearman's rho Correlation coefficient	p value (on correlation with S. Ferritin)
Urea (mg/dl)	-0.091	0.267
Creatinine (mg/dl)	0.003	0.972
eGFR (ml/min/1.73m2)	-0.049	0.549
Urine microalbumin (mg/dl)	0.087	0.292

Of total 150 diabetic patients 26 patients (17.3%) were having nephropathy based on urine microalbumin. Based on nephropathy in patients of T2DM, two groups (A and B) were made. Group A includes patients with nephropathy, while Group B includes patient without Nephropathy.

Parameters	Group A (n=26)		Group B (n=124)		Z value	p value
	Mean	SD	Mean	SD		
Hb (gm/dl)	12.36	1.31	12.99	1.66	-2.379	0.017
TLC (cells/mm3)	8328.44	1921.12	8244.44	1701.79	-0.292	0.770
ANC (cells/mm3)	5433.08	1679.37	5406.72	1324.23	-0.329	0.742
ALC (cells/mm3)	2211.60	655.66	2307.99	719.45	-1.05	0.294
NLR	2.33	1.02	1.96	0.94	-2.134	0.033
MCV (fl)	86.12	5.42	86.39	4.30	-0.337	0.736
S. Ferritin (mg/ml)	177.33	99.88	156.24	126.88	-1.973	0.048

Above table shows the association of hematological indices in patients of Group A (T2DM patients with nephropathy) and Group B (T2DM patients without nephropathy) patients. Mean hemoglobin, MCV and ALC were lower in Group A patients, while TLC, mean ANC and NLR was higher in group A patients. NLR and Serum Ferritin shows significant difference between both groups.

Parameters	Group A (n=26)		Group B (n=124)		Z value	p value
	Mean	SD	Mean	SD		
Urea (mg/dl)	31.51	8.11	26.34	9.27	-3.515	<0.001
Creatinine (mg/dl)	1.12	0.23	0.95	0.23	-4.101	<0.001
eGFR (ml/min/1.73m2)	72.02	18.08	87.13	20.47	-4.75	<0.001

Above table shows the association of Renal function test in patients of Group A (T2DM patients with nephropathy) and Group B (T2DM patients without nephropathy) patients. Mean Urea and Creatinine were higher in group A patients. A significant difference was found in Mean urea and Creatinine level in both groups. While mean eGFR was lower in Group A patients. A significant difference was found in mean eGFR level between both groups.

DISCUSSION

In this study, 150 T2DM patients aged 22 to 78 years were registered; 48.7% of subjects were male, and 51.3% were female.

In our study, the median NLR of the type 2 DM patients was 2.10. This increase probably showed the inflammatory burden of the disease.

In our study, the Mean hemoglobin, MCV, and ALC were lower in Group A (T2DM patients with nephropathy) patients. In contrast TLC, mean ANC and NLR were higher in Group A (T2DM patients with nephropathy). NLR and hemoglobin shows significant difference between both groups.

In the current study, the mean urea and creatinine were higher, while eGFR was lower in Group A (T2DM patients with nephropathy) patients; a significant difference was found in Urea, Creatinine, and eGFR values between both groups.

In the current study, the Mean Serum ferritin levels were higher in Group A (T2DM patients with nephropathy) patients, difference was significant between both groups.

The considerable role of iron overload in the pathogenesis of nephropathy in type 2 DM patients has also been indicated by the observation that the progression of DM to DN can be prevented either by an iron-deficient diet or iron chelators.

CONCLUSION

The results of our study showed that there was a significant relation between NLR, Serum ferritin and DN, suggesting that inflammation and endothelial dysfunction could be an integral part of DN.

Therefore, NLR and S. Ferritin may be considered as a novel surrogate marker of DN in early stages, and should be considered as a predictor and prognostic marker of DN.

One of the limitations of this study is that this was a cross-sectional analysis and sample was relatively small.

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