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Neutrophil - Lymphocyte ratio as a predictive markerfor Early Stage Diabetic Nephropathy

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Abstract

Background: Diabetic nephropathy is a diabetic microvascular complication. An increase in urine albumin excretion is the clinical manifestation. Total white blood cell count is a basic but sensitive measure of inflammation that has been evaluated as an inflammatory marker in a variety of cardiac and noncardiac ailments such as stroke, acute myocardial infarction , and heart failure.

Objective: To analyze Neutrophil-lymphocyte ratio as a predictive marker for early stage diabetic retinopathy.

Methods: The research enrolled 230 individuals, with 115 of them having type 2 diabetes and 69 having Early Stage DN. The control group consisted of 115 healthy volunteers of similar age and gender. All of the patients' samples was collected and tested for HBA1c, CBC, FBS, PPBS, RFT, Urine microalbumin, and Urine albumin creatinine ratio. The Mogensen DN diagnostic criteria and the American Diabetes Association was used

Results: This research had a total of 230 participants. Diabetic nephropathy patients and non-diabetic nephropathy patients were divided into two groups. NLR was shown to have a substantial relationship with neutrophil and lymphocyte counts. In the DN group, mean neutrophil counts increased while mean lymphocyte levels decreased, resulting in a substantially higher NLR value in the patient group than in the control group. The patient group's mean NLR values were considerably higher than the control group's (P 0001), and the NLR values of patients with early stage DN were significantly higher than those of patients without early stage DN (P 0001). The results reveal that DN was associated with NLR, Creatinine, and Insulin Resistance.

Conclusion: NLR might be used as a predictor and predictive risk factor for early-stage diabetic nephropathy. This test is affordable, routinely performed, and easy to compute. NLR can be a cost-effective alternative marker as a predictor of Diabetic Nephropathy in a setting with constrained laboratory resources.

Keywords: Diabetic nephropathy, Inflammation, Microvascular, Urine albumin

Introduction

India is the world's diabetes capital, with diabetes and prediabetes prevalence rates of 9% and 114%, respectively.[1] Indians have an aggressive clinical profile for type 2 diabetic mellitus (T2DM).[2] When compared to Caucasians, Indians had approximately two decades earlier onset of T2DM, as well as the highest rates of prediabetes progression to T2DM (18% in Indians as compared to 2% in the USA, 6% in Finland, and 11 % in China).[3,4]

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Diabetes mellitus is a systemic disease with severe microvascular and macrovascular complications. Diabetic retinopathy, diabetic neuropathy, and diabetic nephropathy are examples of microvascular complications, whereas cardiovascular diseases, stroke, and peripheral vascular disorders are examples of macrovascular complications.[5] Diabetic nephropathy (DN) causes serious complications in 25–40% of diabetic people and is the primary cause of end-stage renal failure.[6] UMAER (urine microalbumin excretion rate) is a test that can be used to detect and track the course of DN.[7]

Inflammation plays a key role in the development and progression of DN, and a number of inflammatory cytokines (interleukin-1 (IL-1), interleukin-6 (IL-6), interleukin-8 (IL-18), tumour necrosis factor (TNF-), and others) are linked to the disease's aetiology.[8] In the case of DM, the CD4/ CD8 ratio decreases. During an inflammatory reaction, the rate of circulating leukocytes changes. Neutrophilia is often accompanied by lymphopenia. [9,10] Neutrophil elevation, which indicates an acute state of inflammation, and lymphopenia, which occurs as a result of physiological stress, have lately been combined into one index.

The high prevalence of diabetes among Indians portends an exponential rise in diabetes-related end organ damage and morbidity over the next few decades. There is a pressing need for low-cost, easy-to-measure predictors of diabetes-related end-organ damage in Indians. This would aid in the implementation of preventative treatment aimed at these patients in order to enhance long-term clinical results.[11] NLR has recently been found as a novel inflammatory marker for evaluating cardiovascular disease severity and poor prognosis in the general population and in patients with ESRD.[12,13]

However, we are aware of just a few research examining the predictive usefulness of NLR in DN. Based on this context, This study intends to evaluate the relationship between diabetic nephropathy and NLR, as well as whether NLR may be used as a predictive and precise indicator.

Material and Methods

This study was a Case Control Study conducted between January 2018 and June 2018 for aduration of 6 months in the Department of General Medicine of R.L.Jalappa Hospital and Research Centre, a tertiary care hospital attached to Sri Devaraj Urs Medical College whichcaters to rural population of Kolar and neighborhood districts.

The study recruited 115 patients diagnosed with type 2 DM, 69 of whom have Early Stage DN. The control group was composed of 115 healthy age and sex matched subjects. A semi structuredquestionnaire which contains age, sex, smoking, family history, chronic diseases, risk factors, dietary compliance and used drugs of each participant was obtained by interviewing after obtaining written informed consent from the eligible subjects.

Inclusion Criteria

- Patients diagnosed with type 2 DM
- Adults > 18 years of age

Exclusion Criteria

- Myocardial infarction
- Coronary artery disease
- Heart failure
- Active infection
- Acute poisoning
- Cancer, AIDS, blood diseases that affect neutrophils and lymphocytes
- Diseases that affect urinary protein excretion
- Diseases that affect the renal blood flow

Controls: The control group was composed of healthy age and sex matched subjects.

Blood samples were drawn from all the patients and were subjected to CBC, HBA1c, FBS, PPBS,RFT, Urine micro albumin and Urine albumin creatinine ratio. The American Diabetes Associationand the Mogensen DN diagnostic criteria state that DM patients with urinary albumin excretion ratios (UAE) reaching 20 µg/min to 200 µg/min or 30 mg/24 h to 300 mg/24 h more than twice in6 months have early stage DN.

Statistical Analysis: SPSS statistical software version 24.0 was used for statistical calculations. The $P < 0\cdot05$ was considered statistically significant.

Ethical considerations: Prior to the onset of the study, ethical approval was obtained from ethical committee of Mahavir Institute Of Medical Sciences. All the collected information was kept confidential, and it is being used for research purpose only.

Observation and Results

This research had a total of 230 patients. Diabetic nephropathy patients and non-diabetic nephropathy patients were divided into two groups.

Table 1. Distribution based on Demographic and laboratory data of the patient and control groups

Variable	DN group (n =115)	Control group (n =115)	p-value
Age (years)	52·21 ± 8·47	51·19 ± 10·73	0.34
Male	67 (58.2)	59 (51.3)	0.12
Female	48(42.8)	56 (48.7)	
BMI (kg/m2)	25·13 ± 3·93	24·24 ± 3·41	0·069
UA (µmol/l)	304·61 ± 108·81	331·59 ± 81·93	0·083
Creatinine (µmol/l)	82·41 ± 19·67	73·91 ± 18·39	0·026*
TG (mmol/l)	2·30 ± 2·46	1·26 ± 0·69	0·004*
Total cholesterol (mmol/l)	5·80 ± 7·17	4·89 ± 0·92	0·232
HDL (mmol/l)	1·54 ± 0·73	1·41 ± 0·27	0.37
LDL (mmol/l)	3·01 ± 0·93	2·91 ± 0·78	0.41

In both the groups the mean age, gender, BMI, was nearly similar. Early Stage DN was found in 69 of the 115 patients with DM (60%). The patient group showed significantly higher creatinine and triglyceride (TG) values than the control group. No statistically significant differences in UA, TC, HDL, and LDL levels were detected between the patient and control groups.

Table 2: Comparison of Laboratory Parameters between and within the groups

Variables	Patients with diabetes			
	With early stageDN (n = 69)	Without earlystage DN (n =46)	Control group(n = 115)	p- value
WBCs (109/l)	6·74 ± 1·99	5·39 ± 1·56	6·61 ± 1·67	<0·001*
Neutrophils (109/l)	4·39 ± 1·51	3·81 ± 1·33	3·72 ± 1·27	<0·001*
Lymphocytes (109/l)	1·91 ± 0·85	1·81 ± 0·89	2·03 ± 0·47	0·023
Monocytes (109/l)	0·43 ± 0·12	0·46 ± 0·17	0·51 ± 0·19	0.028
Platelets (109/l)	195·31 ± 46·53	204·82 ± 52·87	211·32 ± 51·27	0.19
CRP (mg/l)	2·29 ± 1·03	1·74 ± 0·89	0·99 ± 0·81	<0·001*
NLR	2·51 ± 0·63	2·12 ± 0·68	1·73 ± 0·69	<0·001*

NLR was shown to have a substantial relationship with neutrophil and lymphocyte counts. In the DN group, mean neutrophil levels have increased while mean lymphocyte levels decreased, resulting in a substantially higher NLR value in the patient group than in the control. The patient group's mean NLR values were considerably higher than the control group's, and the NLR values of patients with early stage DN were significantly higher than those of patients without early stage DN (P<0001).

Table 3: Logistic regression analysis of factors independently associated with DN

Variables	P	EXP(B)	95% CI
NLR	0·002	2·081	1·267–3·441
Creatinine	<0·001	1·028	1·031–1·063
Total cholesterol	0·011	1·532	1·134–1·899
TG	0·387	0·953	0·809–1·079
SBP	0·017	1·087	1·039–1·142
DBP	0·157	1·021	0·959–1·123
Smoking	0·071	1·945	0·981–3·790
BMI	0·078	0·812	0·823–1·029
HbA1c	0·058	1·173	1·009–1·391
Insulin Resistance	<0·001	1·156	1·051–1·271

The risk variables were subjected to a logistic regression analysis. NLR, Creatinine, and Insulin Resistance were all associated with DN.

Discussion

The purpose of this study was to look at the independent link between NLR and DN. The NLR levels in diabetic patients with DN were substantially higher than in diabetic patients without DN and healthy controls. DN is a typical DM complication that comprises vascular and neuropathic complications. Many epidemiological studies have found that diabetes is associated to chronic inflammation, which can contribute to the development of angiopathy and nephropathy. The cause of DN, a common serious consequence in diabetic individuals, is unknown. DN has been associated with chronic inflammation in several studies. [14,15,16] Insulin resistance, diabetes, and related microvascular and macrovascular complications are known to be influenced by inflammatory chemicals and endothelial dysfunction.[17] In earlier Caucasian research, neutrophililia and relative lymphocytopenia were

found to be independent indicators of nephropathy, neuropathy, and retinopathy.[18,19,20,21] However, there are no comparable data on the effectiveness of NLR in Indians with diabetes. NLR can be an economical and accurate predictor of the incidence of early stage diabetic nephropathy in Indians with T2DM.

The findings of this study corroborate with Huang et al., who observed that NLR was considerably higher in diabetics patients with signs of nephropathy.[22]

NLR was considerably increased in individuals with higher albuminuria, showing a correlation between inflammation and endothelial dysfunction in diabetics with nephropathy, according to Akbas et al.[23] NLR has been associated to diabetic nephropathy and is also a predictor of end-stage renal disease, according to Afsar et al.[24] NLR was emphasised to be a predictive factor for a decrease in renal function in a three-year follow-up study of diabetic individuals.[25] NLR levels were also shown to be considerably greater in diabetic patients with nephropathy compared to diabetic patients without microvascular problems and healthy control participants, according to Moursy et al.[26] NLR was also shown to be associated with albuminuria in a study of Turkish patients.[27] Tsai et al. observed significant differences in total leucocyte, neutrophil, and monocyte counts between diabetics and healthy individuals. They also reported that in the presence of ischemic problems, NLR is much higher.[28] The NLR levels in diabetic patients were greater than those in healthy controls. Early stage DN was shown to be much more common in diabetes individuals with high NLR values than in diabetic patients with low NLR values.

Conclusion

According to the findings of this study, NLR may be used as a predictor and prognostic risk marker of early stage diabetic nephropathy . Further research is needed to develop substantial proof to be used more routinely in clinical settings. NLR is a simple and clear metric. This test is affordable and performed on a regular basis. In a setting with limited laboratory resources, NLR can be a low-cost, effective alternative marker for predicting diabetic nephropathy.

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Conflict of interest: Nil

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