Original Article

Role of Neutrophil / Lymphocyte Ratio in Diabetes 2 Nephropathy

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ABSTRACT

Objective: To study the role of Neutrophil / lymphocyte ratio in diabetes 2 nephropathy

Study Design: Observational / cross sectional Study

Place and Duration of Study: This study was conducted at the Rawal Institute of Medical Sciences Rawalpindi and Idris Teaching Hospital Sialkot during Feb 2018 to Feb 2020.

Materials and Methods: It is an observational cross-sectional study. Totally 115 diagnosed type 2 diabetes mellitus patients were registered in this study. NLR was calculated by analyzing differential leukocyte count in complete blood picture. Albuminuria was tested by MICRAL-II TEST strips by dipstick method. Demographic data and laboratory Investigations were recorded on designed Performa. Informed written consent was taken from every patient before collecting the sample, history and examination. Permission of Ethical Committee of the Institute was considered for collection of data and get publishing in medical journal.

Results: Totally 115 diabetic patients were registered. About 56 patients had DN and 59 had normal urine albumin. Mean NLR for a normal group is 1.94 ± 0.65 and in DN group is 2.83 ± 0.85 which was highly significant ($P < 0.001$). Estimated glomerular filtration rate ($P = 0.047$) and serum glutamate pyruvate transaminase ($P < 0.001$) were also significant.

Conclusion: The results of our study show that there was a significant relation between NLR and DN. Therefore, NLR may be considered as a novel surrogate marker of DN in early stages.

Key Words: Diabetic nephropathy, inflammation, microvascular, neutrophil-lymphocyte ratio, urine albumin

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INTRODUCTION

Diabetes mellitus is a fundamental infection having genuine microvascular and macrovascular entanglements. Microvascular intricacies incorporate diabetic nephropathy (DN), diabetic retinopathy, and diabetic neuropathy while macrovascular confusions incorporate stroke, cardiovascular ailments (CVDs), and fringe vascular diseases.[1]

DN is a typical miniaturized scale angiopathic inconvenience in patients with diabetes. DN is one of the most well-known reasons for end-stage renal illness (ESRD).[2] DN is clinically showed as expanded egg whites urea discharge beginning from microal-buminuria to macroalbuminuria and in the long run ESRD.[3] However, the level of albuminuria isn't really connected to infection movement in patients with DN related with either type 1 or type 2 diabetes mellitus (T2DM).[4,5] In type 1 diabetes, when clear DN creates, there is persevering proteinuria, and movement toward ESRD must be eased back yet couldn't be stopped.[6,7] Due to this, there is a need of early indicators of DN by which we can foresee the sickness and can end the movement of the ailment. The Asian Indian populace has more commonness of DN when contrasted with the Caucasian population.[8]

A few investigations that have investigated the connection between fundamental irritation and vascular infection showed that constant aggravation advances the turn of events and quickening of small scale and full scale angiopathic intricacies in patients with diabetes. All out white platelet (TWBC) tally is a rough however delicate pointer of aggravation which should be possible effectively in research center routinely. It is a financially savvy examination. Increment in the neutrophil include is found in blood clot development and ischemic ailments. The neutrophil-lymphocyte proportion (NLR) in complete blood include is concentrated in numerous cardiovascular and noncardiac infections as a fiery marker and is utilized to anticipate the forecast of sicknesses, for example, intense myocardial dead tissue (MI), stroke, and cardiovascular breakdown.

DN in T2DM has a provocative pathology. Numerous incendiary markers have been seen as identified with DN, for example, interleukin-1 (IL1), IL6, IL8, changing development factor beta 1, tumor rot factor-

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alpha (TNF-α), and cytokines. Notwithstanding, their estimation isn't utilized routinely as it is difficult to do it.[9,10] In this regard, NLR has developed as a novel substitute marker.

In the current investigation, the relationship of NLR with DN in Indian patients is examined, regardless of whether NLR can be utilized as a substitute marker of DN in this populace.

MATERIALS AND METHODS

It is an observational cross-sectional study. This study was conducted at the Rawal Institute of Medical Sciences Rawalpindi and Idris Teaching Hospital Sialkot during Feb 2018 to Feb 2020. Totally 115 diagnosed type 2 diabetes mellitus patients were registered in this study. NLR was calculated by analyzing differential leukocyte count in complete blood picture. Albuminuria was tested by MICRAL-II TEST strips by dipstick method.

RESULTS

In this study, diagnosed T2DM patients were screened for DN.

A total of 115 diabetic patients were registered. Of these, 56 patients had DN and 59 had normal urine albumin. All these patients were similar in their age distribution, dietary habits, smoking, and other profiles. These groups were compared for various variables such as age, BMI, WHR, BP, total leukocyte count, absolute Neutrophil count (ANC), absolute lymphocyte count (ALC), NLR, serum creatinine, blood urea, serum glutamate pyruvate transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), FBS, PPBS level, and HbA1c.

In the present study, the mean age of patients of normal group and DN group was 52.29 ± 11.45 years and 50.05 ± 11.29 years, respectively. Both groups had similar distribution of age (P = 0.294). In addition, there was no sex-related variability (in normal group, male = 26, female = 33, and in DN group, male = 25, female = 31) (P = 0.951). Metabolic and laboratory parameters such as and glycemic parameters (blood sugar level [BSL] fraction unbound in the plasma FBS, BSL PPBS, HbA1c) were compared in both groups and are shown in Table 1. There was a significant difference between the normal group and DN group with relation to NLR (P < 0.001), but individually, the TWBC count did not differ in the two groups [Table 2]. There was also a significant difference between normal group and DN group with relation to ANC (P < 0.001) and ALC (P < 0.001) [Table 2]. In the present study, renal function tests of all patients were carried out, and estimated GFR (eGFR) was calculated by CKD-EPI formulae. In relation to eGFR, there was a significant difference between the two groups (P = 0.047) [Table 3]. Patients with albuminuria had a significantly low eGFR (mean eGFR = 85.71 ± 27.72) than the normal group (mean eGFR = 96.2 ± 28.23). However, other investigations such as blood urea and serum creatinine had no difference in these two groups [Table 3]. LFTs for all patients were carried out, and SGPT (mean SGPT = 40.89 ± 36.62) was found to be significantly raised in DN patients' group as compared to normal patients' group (mean SGPT = 9.74 ± 13.03), which was highly statistically significant (P < 0.001) [Table 4]. In reference to glycemic parameters, we did not observe any significant difference with respect to FBS (P = 0.0769), PPBS (P = 0.5674), and HbA1c (P = 0.06) in the two groups, i.e., normal diabetic patients and patients with DN. In our study, by applying linear regression analysis, we found HBA1c as a risk factor for DN.

Table No 1. Comparison of demographic and laboratory parameters of diabetic patients

Variable	Patients with albuminuria (n=61)	Patients without albuminuria (n=71)	P
Age	53.00 +- 11.23	51.05 +- 11.21	0.2842
Gender			
Female	31	33	0.851
Male	30	38	
Hb (g %)	12.00 +- 1.23	12.23 +- 1.65	0.0975
FBS	172.45 +- 40.99	159.14 +- 40.99	0.089
PPBS	199.13 +- 46.23	196.17 +- 41.99	0.3421
BSL FUP FBS	147.17 +- 22.9	139.4 +- 21.93	0.0689
BSL PPBS	178.27 +- 19.69	176.1 +- 19.52	0.5672
Hba1c	8.47 +- 1.49	7.78 +- 1.15	0.0599

Hb: Hemoglobin, FBS: Fasting Blood Sugar, HbA1c: Glycated Hemoglobin, PPBS: Postprandial Blood sugar, BSL: Blood Sugar Level

Table No.2: Neutrophil-lymphocyte ratio and other laboratory parameters of diabetic patients

Variable	With nephropathy	Without nephropathy	P
NLR	2.82 +- 0.83	1.93 +- 0.63	0.00001
TLC	7579.35 +- 1882.43	7383.73 +- 1444.99	0.5320
ANC	5292.90 +- 1478	4652.52 +- 1184.93	0.0115
ALC	1946.99 +- 579.79	2448.99 +- 579.79	<0.001

NLR: Neutrophil-lymphocyte ratio, TLC: Total leukocyte count, ANC: Absolute Neutrophil count, ALC: Absolute lymphocyte count Statistically significant (p<0.05).

Table No.3: Renal function test of diabetic patients

Variable	With nephropathy	Without nephropathy	P
Serum Urea	29.43 +- 14.73	25.37 +- 11.82	0.1051
Serum Creatinine	0.87 +- 0.32	0.78 +- 0.25	0.0791
GFR	85.70 +- 27.70	95.99 +- 27.79	0.046

Statistically significant (p<0.05). GFR Glomerular filtration rate

Table No.4: Liver function test of diabetic patients

Variable	With nephropathy	Without nephropathy	P
Bilirubin	4.91 +- 1780	0.62 +- 0.19	0.0672
SGPT	40.87 +- 17.06	28.99 +- 13.00	<0.001
SGOT	41.19 +- 36.59	32.11 +- 12.90	0.825

Statistically significant (p<0.05). SGPT: Serum glutamate pyruvate transaminase, SGOT: Serum glutamatc oxaloacetic transaminase

DISCUSSION

The key finding of this examination was that NLR levels were seen as essentially related (P = 0.001) with patients who were determined to have beginning time DN when contrasted with those with typical egg whites levels. This investigation is one of the first in Quite a while to survey the connection between NLR andcomplications.[10]

NLR is a novel marker of interminable irritation that displays a parity of two reliant segments of the insusceptible framework; neutrophils that are the dynamic vague incendiary go between structures the principal line of resistance though lymphocytes are the administrative or defensive part of inflammation.[11]

In CKD patients, NLR has demonstrated to be a simple and reasonable lab boundary that gives huge data with respect to irritation. Besides, in a 3-year follow-up investigation of diabetic patients, NLR filled in as an indicator of intensifying renal function. Afsar has demonstrated that NLR could be identified with DN and is likewise associated as a pointer of ESRD.[12] In another examination, Akbas et al. have indicated that NLR was essentially raised in patients with expanded albuminuria highlighting a connection among irritation and endothelial brokenness in diabetics with nephropathy.[13]

So also in our examination, the mean NLR among diabetic patients with albuminuria (2.83 ± 0.85) was altogether higher than among those without albuminuria (1.94 ± 0.65). Furthermore, ANC and ALC levels were additionally seen as essentially corresponded with patients with albuminuria. In concordance with our outcomes, Huang et al. have additionally discovered that NLR esteems were fundamentally higher in diabetic patients with proof of nephropathy (2.48 ± 0.59) than in diabetic patients without nephropathy (2.20 ± 0.62) and solid controls (1.80 ± 0.64). ANC and ALC levels were additionally found to correspond with DN in their examination.[14] In addition, an ongoing report in Egyptian patients has demonstrated by Moursy et al that NLR esteems were fundamentally higher in diabetic patients with retinopathy (P < 0.001), neuropathy (P = 0.025), and nephropathy (P < 0.001) than those of diabetic patients with no microvascular inconveniences and solid controls.[15] Another as of late distributed investigation in Turkish patients has likewise demonstrated by Kahraman C, et al that NLR levels altogether expanded in corresponding to albuminuria levels in diabetic patients.[16]

There was no critical connection among's typical and DN bunches corresponding to age, sex, BMI, WHR, Hb, absolute cholesterol, LDL, TG, HDL, and VLDL as saw in the current investigation despite the fact that there was noteworthy contrast among the two gatherings in regard to eGFR values (P = 0.047). Patients with albuminuria had altogether low eGFR (mean eGFR = 85.71 ± 27.72) when contrasted with those patients with typical egg whites levels (mean eGFR = 96.2 ± 28.23). eGFR is one of the most explicit boundaries for kidney function.[17] if there should be an occurrence of DN, eGFR diminishes as sickness advances. There were no critical intergroup contrasts for either blood urea or serum creatinine levels.

Concerning glycemic boundaries, there were no noteworthy contrasts between the two gatherings, comparable to FBS, PPBS, or HbA1c however different examinations have demonstrated HbA1c to be a free hazard factor for DN.[18] On applying straight relapse investigation in the current examination, HbA1c was additionally seen as an indicator for DN.

One of the constraints of this examination is this was a cross-sectional investigation and the example size was generally little. Since this was not an imminent controlled examination, any definitive causal relationship among NLR and DN couldn't be explored.

CONCLUSION

The results of our study show that there was a significant relation between NLR and DN. Therefore, NLR may be considered as a novel surrogate marker of DN in early stages.

Author's Contribution:

Concept & Design of Study:	M Husain Bloch
Drafting:	Faisal Iqbal
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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Rathmann W, Giani G. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27: 2568–9.
2. Ritz E, Rychlík I, Locatelli F, Halimi S. End-stage renal failure in type 2 diabetes: A medical catastrophe of worldwide dimensions. Am J Kidney Dis 1999;34:795–808.
3. Chronic Kidney Disease Surveillance System. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services; 2011. [Last accessed on 2016 Nov 19]. Centers for Disease Control and Prevention. Available from:
4. Evans T, Capell P. Diabetic Nephropathy. [Last accessed 2017 Mar 21]. Available from:
5. Perkins BA, Ficociello LH, Roshan B, Warram JH, Krolewski AS. In patients with type 1 diabetes and new-onset microalbuminuria the development of advanced chronic kidney disease may not require progression to proteinuria. Kidney Int 2010;77: 57–6.
6. KDIGO. Chapter 1: Definition and classification of CKD. [Last accessed on 2016 Nov 19];Kidney Int Suppl 2013 3:19.
7. Shiny A, Bibin YS, Shanthirani CS, Regin BS, Anjana RM, Balasubramanyam M, et al. Association of neutrophil-lymphocyte ratio with glucose intolerance: An indicator of systemic inflammation in patients with type 2 diabetes. Diabetes Technol Ther 2014;16:524–30.
8. 8 Akpek M, Kaya MG, Lam YY, Sahin O, Elcik D, Celik T, et al. Relation of neutrophil/lymphocyte ratio to coronary flow to in-hospital major adverse cardiac events in patients with ST-elevated myocardial infarction undergoing primary coronary intervention. Am J Cardiol 2012;110:621–7.
9. Öztürk ZA, Kuyumcu ME, Yesil Y, Savas E, Yildiz H, Kepekçi Y, et al. Is there a link between neutrophil-lymphocyte ratio and microvascular complications in geriatric diabetic patients? J Endocrinol Invest 2013;36:593–9.
10. Okyay GU, Inal S, Oneç K, Er RE, Pasaoglu O, Pasaoglu H, et al. Neutrophil to lymphocyte ratio in evaluation of inflammation in patients with chronic kidney disease. Ren Fail 2013;35:29–36.
11. Azab B, Daoud J, Naeem FB, Nasr R, Ross J, Ghimire P, et al. Neutrophil-to-lymphocyte ratio as a predictor of worsening renal function in diabetic patients (3-year follow-up study) Ren Fail 2012; 34:571–6.
12. Afsar B. The relationship between neutrophil lymphocyte ratio with urinary protein and albumin excretion in newly diagnosed patients with type 2 diabetes. Am J Med Sci. 2014;347:217–20.
13. Akbas EM, Demirtas L, Ozcicek A, Timuroglu A, Bakirci EM, Hamur H, et al. Association of epicardial adipose tissue, neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio with diabetic nephropathy. Int J Clin Exp Med 2014;7: 1794–801.
14. Huang W, Huang J, Liu Q, Lin F, He Z, Zeng Z, et al. Neutrophil-lymphocyte ratio is a reliable predictive marker for early-stage diabetic nephropathy. Clin Endocrinol (Oxf) 2015;82: 229–33.
15. Moursy EY, Megallaa MH, Mouftah RF, Ahmed SM. Relationship between neutrophil lymphocyte ratio and microvascular complications in Egyptian patients with type 2 diabetes. Am J Intern Med 2015;3:250–5.
16. Kahraman C, Kahraman NK, Aras B, Cosgun S, Gülcan E. The relationship between neutrophil-to-lymphocyte ratio and albuminuria in type 2 diabetic patients: A pilot study. Arch Med Sci 2016;12:571–5.
17. Levey AS, Inker LA, Matsushita K, Greene T, Willis K, Lewis E, et al. GFR decline as an end point for clinical trials in CKD: A scientific workshop sponsored by the National Kidney Foundation and the Us Food and Drug Administration. Am J Kidney Dis 2014;64: 821–35.
18. Alkhouri N, Morris-Stiff G, Campbell C, Lopez R, Tamimi TA, Yerian L, et al. Neutrophil to lymphocyte ratio: A new marker for predicting steatohepatitis and fibrosis in patients with nonalcoholic fatty liver disease. Liver Int 2012; 32:297–302.