NEUTROPHIL LYMPHOCYTE RATIO AS AN EVALUATION TOOL FOR THE GLYCEMIC CONTROL IN PATIENTS SUFFERING FROM DIABETES

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Abstract:
Objective: Enhanced neutrophil lymphocyte ratio is the predictor and identifier for many cardiac as well as non-cardiac complications. The purpose of this study is to evaluate the association between neutrophil lymphocyte ratio and various glycemic control levels in the patients suffering from Type-2 diabetes.
Methodology: This is an observational research work conducted at Lahore General Hospital from November 2018 to April 2019. In this research work, 330 diabetic patients were separated into 3 groups depending upon the control of diabetes in accordance with the criteria defined by ADA. Group-A contains the patients with $HbA1c \leq 7.0\%$ with excellent control, Group-B HbA1c 7.0 to 9.0 % with poor control and Group-C $HbA1c \geq 9.0\%$ with worst control. We evaluated the patients in terms of C-reactive protein and count of complete blood.
Results: Comparison of the Group-A patients with the patients of Group-C displayed a high count of leukocyte (P: 0.001), high count of neutrophil (P: 0.003) and lower count of lymphocyte (P: 0.440) whereas patients in Group-B were not significant different. In the same manner, neutrophil lymphocyte ratio value was much high in the patients of Group-C in comparison with the patients of Group-B and Group-A (4.30 ± 2.80, 2.70 ± 1.0 and 2.0 ± 0.50 (P: 0.001). We discovered the neutrophil lymphocyte ratio as an independent predictor of the adverse control of diabetes (OR= 1.8090, 95.0% CI= 1.459 to 2.401) along with FBS (Fasting Blood Sugar) (OR= 0.9380, 95.0% CI= 0.995 to 0.982) and CRP (OR= 1.02, 95.0% CI= 1.003 to 1.028).
Conclusion: Enhanced level of neutrophil lymphocyte ratio has association with the increased HbA1c and adverse glycemic control among patients suffering from Type-2 Diabetes Mellitus. This tool can be used as a disease monitoring tool in the duration of the follow up period of the patients.
KEYWORDS: Neutrophil Lymphocyte Ratio, Blood Count, Neutrophil. Diabetes Mellitus.

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INTRODUCTION:

Diabetes Mellitus is a preventable disorder of metabolism and it is known as silent in the whole world because majority of the patients remain without symptoms until they develop complications. Urbanization, sedentary style of life and transition of the lower countries have given a rise to the prevalence of this disease [1]. There is an estimation that the rise of diabetes in the countries of South Asia is more than hundred percent. There is requirement of drastic steps through different programs of health awareness to control the increasing trend of diabetes to reduce the health burden [2]. Different research works have discovered that enhanced counts of leukocyte are trustworthy markers of systemic inflammation and this is a good marker for various complications associated with diabetes [3, 4]. There is high concern about value of neutrophil lymphocyte ratio now a day which is an identifier for the determination of different complications because it has high prognostic ability in comparison with the count of the white blood cells. Furthermore, predictive neutrophil lymphocyte ratio value is highly comparable with different markers like CRP (C - reactive protein), TNF-α (Tumor Necrosis Factor) and IL-6 (Interleukin) in the identification of the sub-clinical inflammation and endothelial abnormality in different research works [5, 6].

There are many advantages of neutrophil lymphocyte ratio on other markers as wide availability, less expensive, reliability and easy detection in laboratory. Even patients present with high value of neutrophil lymphocyte ratio but normal count of TLC can have high risk of diseases related to atherosclerosis [7-9]. HbA1c test tells about the hyperglycemia's severity and it is best bio-marker for various complications related with diabetes [10]. But its preciseness is much lower than the neutrophil lymphocyte ratio. Current research work aimed to evaluate the association between glycemic control and neutrophil lymphocyte ratio in terms of comparison in 3 groups.

METHODOLOGY:

This observational research work carried out at Lahore General Hospital from November 2018 to April 2019. We took the verbal consent from all the patients of this research work after explaining them the purpose of this research work. Ethical committee of our institute gave the permission to conduct this research work. In the start, we recruited total 580 patients under follow-up of their Type-2 Diabetes Mellitus. but 330 patients fulfilled our inclusion standard. We divided the patients into three groups according to criteria prescribed by ADA. Excellent control group made the Group-A with HbA1c ≤ 7.0%, Group-B with HbA1c 7.0% to 9.0% having poor control and Group-C HbA1c ≥ 9.0% having worst control respectively. We carried out complete examination of the patients as well as their history and the causes which have influence on inflammation. Patients suffering from other serious complications were not the art of this research work. We also gathered the complete background data about cigarette smoking, use of alcohol and other drugs which can affect inflammation.

We gathered the blood samples of the patients after fasting of complete twelve hours. We used the automatic hematology analyzer for the measurement of TLC (Total Leukocyte Counts). We estimated the neutrophil lymphocyte ratio with the division of absolute ratio of neutrophil to the absolute ratio of lymphocyte. We also measured the HbA1c level with standard procedure. SPSS V. 20 was in use for the statistical analysis of collected information. We present the categorical data in frequencies and percentages. We used ANOVA test for the presentation of comparison among patients of all 3 groups.

RESULTS:

Characteristics of demography and hematological factors at baseline of Group-A, Group-B and Group-C are present in Table-1. We found no statistical significant disparities regarding age, gender, past history of family and diabetes duration in the patients of all 3 groups. But serum glucose (P= 0.0040) and body mass index (P=0.0020) were much high in the patients of Group-C.

Table-I: Baseline Characteristics Of Three Groups

Parameters	Group A		Group B		Group C		P Value
	Mean / No	SD / Percent	Mean / No	SD / Percent	Mean / No	SD / Percent	
Age (years)	62.6	13.00	64.6	15.90	60.4	12.70	0.2260
Male (n-%)	52.0	74.00	48.0	68.00	54.0	77.00	0.3750
BMI (kg/m^2)	26.5	2.80	27.2	3.20	29.2	3.80	0.0020
Diabetes >10years	14.0	20.00	17.0	24.00	19.0	27.00	0.5020
Family history of CAD	15.0	21.00	12.0	17.00	16.0	23.00	0.4040
Glucose (mg/dl)	106.0	24.20	124.0	45.80	152.0	65.40	0.0040
Hemoglobin g/dl	12.8	1.84	12.7	2.23	13.1	1.50	0.3920
Platelets count*	245.0	85.00	254.0	76.00	249.0	80.00	0.3900
WBC count	7.4	2.10	8.6	3.60	9.8	2.80	0.0010
Neutrophil count	4.6	2.40	5.6	3.20	7.4	2.80	0.0010
Lymphocyte count	2.3	0.80	2.3	0.70	2.0	0.90	0.4400
Neutrophil Lymphocyte Ratio	2.0	0.50	2.7	1.00	4.3	2.80	0.0010
CRP	0.8	0.92	2.6	0.42	4.4	0.54	0.0030

We found the similar count of hemoglobin and platelets in the patients of all three groups. In comparison to the patients of Group-A, patients of Group-c displayed the high count of leukocyte (P= 0.0010), high count of neutrophil (P= 0.0030) and low count of lymphocyte (P= 0.440) whereas patients of Group-B were not different. Neutrophil Lymphocyte Ratio value was also much high in the patients of Group-B and Group-A (4.30 ± 2.80, 2.70 ± 1.0 and 2.0 ± 0.50 respectively P= 0.0010) as presented in Table-1.

Multivariate analysis displayed that high neutrophil lymphocyte ratio level was independent predictor of the adverse control of diabetes (Group-C) (OR= 1.8090, 95.0% CI= 1.4590 to 2.4010) along with FBS (OR= 0.9380, 95.0% CI= 0.995 to 0.982) and CRP (OR= 1.02, 95.0% CI- 1.003 to 1.028) as presented in Table-2.

Table-II: Regression Analysis Association With Worst Diabetic Control

Variables	Odds Ratio	%95 confidence interval	P value
Neutrophil Lymphocyte Ratio	1.8090	(1.4590 - 2.4010)	< 0.0010
Glucose mg/dl	0.9380	(0.9950 - 0.9820)	0.0210
BMI	1.9050	(0.4530 - 9.6440)	0.5890
CRP	1.0200	(1.0030 - 1.0280)	0.0010

DISCUSSION:

In this current research work, we discovered a positive association among neutrophil lymphocyte ratio value and level of HbA1c. This is first research work based on observations to examine the influence of neutrophil lymphocyte ratio on various values of glycemic control depending upon the values of HbA1c in patients of Type-2 Diabetes Mellitus and their comparison with CRP. We can easily calculate the neutrophil lymphocyte ratio with normal blood test with the division of absolute ratio of neutrophil to the absolute ratio of lymphocyte. This is much reliable than the complete count of blood in the identification of sub-clinical inflammation in cardiac and non-cardiac complications. Different research works have displayed that neutrophil lymphocyte ratio has better diagnostic and prognostic potential for various diseases related with atherosclerosis in which Diabetes Mellitus is much important [11, 12]. There was a dominant role of neutrophil lymphocyte ratio in different research works performed on patients suffering from Diabetes Mellitus. Shiny [13] and Lou [14] discovered that there is strong association of increased neutrophil lymphocyte ratio with the intolerance to glucose and resistance to insulin in patients of Type-2 Diabetes Mellitus. various research work confirmed that neutrophil lymphocyte ratio value has a suitable predictive marker of diabetic nephropathy, diabetic foot ulcer and retinopathy [15, 6, 7].

Furthermore, enhanced neutrophil lymphocyte ratio is predictor of important cardiovascular incidents in patients of coronary artery diseases and acute

coronary syndrome and it also has association with enhanced thickness of carotid artery intima-media in patients of Type-2 Diabetes Mellitus [8, 9]. There is very limited information available to find out the impact of neutrophil lymphocyte ratio on insulin resistance. Selfil discovered that enhanced neutrophil lymphocyte ratio may have association with increased HbA1c in patients of Type-2 Diabetes Mellitus [10]. Oh [21] and Demirtas [2] showed relationship between glycemic control and indices of hematology in the patients of Diabetes Mellitus and also concluded the neutrophil lymphocyte ratio value as an identifier of complications in the follow-up duration of diabetic patients. Current research work confirmed that hyperglycemia has strong association with the enhanced neutrophil lymphocyte ratio. Even in current research work, we discovered a strong association between CRP and neutrophil lymphocyte ratio in the patients available with adverse control of diabetes. There are many research works investigating the increased CRP association with the white blood cells for control of glucose level [13-14]. This current research work displayed that neutrophil lymphocyte ratio can evaluate various levels of glycemic control and high level of neutrophil lymphocyte ratio can predict the incoming complications in the follow-up period of Type-2 diabetes mellitus.

CONCLUSION:
Values of neutrophil lymphocyte ratio are the well evaluation tool of various glycemic control levels in patients of Type-2 diabetes mellitus. High values of neutrophil lymphocyte ratio are the predictor of adverse diabetic control. Therefore, it can be utilized as a monitoring tool of disease in the follow-up period of diabetics.

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