

Relationship in NLR (Neutrophil Lymphocyte Ratio and IR (Insulin Resistance) among Patients Diagnosed with Type II Diabetes

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Abstracts

Higher neutrophil and lower lymphocyte counts are hallmarks of the immunological response to different physiological stresses, and NLR is frequently identified as an inflammatory marker to gauge the severity of the illness. A simple yet affordable, easily accessible, and sensitive measure of the state of inflammation is the white blood cell (WBC) count. WBCs have a favorable correlation with inflammation, especially in heart conditions. A rise in neutrophil counts is linked to ischemia damage and thrombus development. The link between NLR and IR in the general population and with regard to insulin use has not, as far as we know, been studied. The association between IR and NLR would need to be found through this present study. The study is based on secondary data and carries retrospective research design. Sample of the study is 500 patients from Diabetes Center of King Abdulaziz Hospital in Jeddah city, Saudi Arabia. SPSS Ver. 22.0 was used to analyze the collected data.

Keywords: Relationship in NLR and IR, Type 2 Diabetes, Diagnosis.

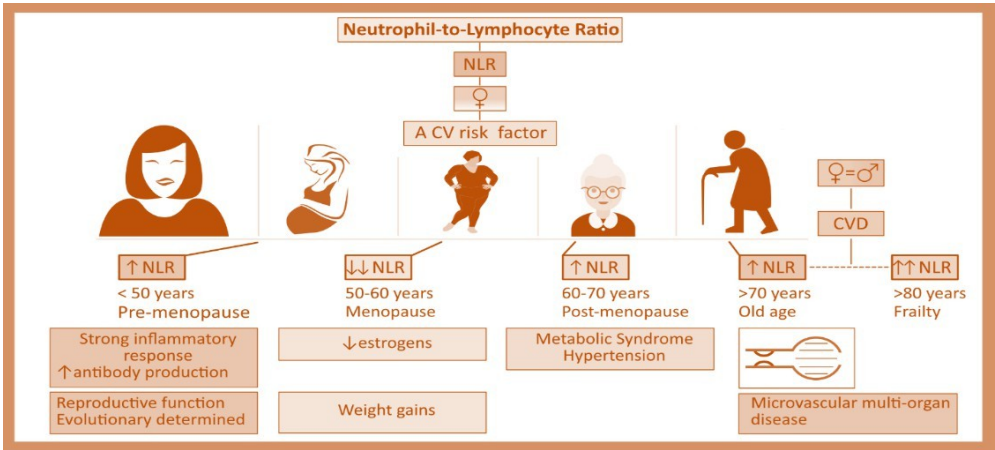
1. Introduction

Insulin resistance is a hallmark of type 2 diabetes mellitus (T2DM), which is linked to diabetes and heart disease. Heald et al (2020) Chronic inflammation causes diabetic microangiopathy to develop more quickly in addition to diabetes patients developing macroangiopathy, according to a number of research that examined the connection between systemic inflammation and cardiovascular disorders. Diabetes, obesity, dyslipidemia, hypertensive disorders, and poor glucose tolerance are all thought to be caused by insulin resistance (IR), which is a decrease in the body's response or sensitivity to insulin. Trtica et al (2020); Harris et al (2020) IR syndrome, which Zimmet et al. renamed metabolic syndrome in 1997, is linked to several metabolic illnesses. Although the precise molecular mechanism causing insulin resistance (IR) is still unknown, a number of studies have established the link between insulin resistance and systemic inflammation, where a compromised immune system is a key factor in the development of diabetes mellitus. Higher neutrophil and lower lymphocyte counts are hallmarks of the immunological response to different physiological stresses, and NLR is frequently identified as

an inflammatory marker to gauge the severity of the illness. A simple yet affordable, easily accessible, and sensitive measure of the state of inflammation is the white blood cell (WBC) count. WBCs have a favorable correlation with inflammation, especially in heart conditions. A rise in neutrophil counts is linked to ischemia damage and thrombus development.

WBC subtypes may represent many facets of inflammatory or infectious processes. Recent research has demonstrated that in individuals with acute heart failure, the presence of neutrophilia and relative lymphopenia is an independent predictor of mortality. Cole et al (2020) Furthermore, NLR was presented as a new indicator to assess inflammation in both cardiac and noncardiac conditions. Studies assessing the predictive usefulness of NLR in IR, particularly in individuals with recently diagnosed diabetes, are scarce, nonetheless. The choice of recently diagnosed diabetes participants is the key to this investigation. Sun et al (2020) Our goal is to employ NLR to assess the connection between inflammation and IR and ascertain whether NLR is a valid and predictive sign. Sharma et al (2022); Misirlioglu et al (2024)

NLR does not necessarily indicate insulin resistance, even though it has a strong correlation with metabolic syndrome. An association between IR and NLR was shown in a prior study with diabetic patients. They had DM patients with IR and DM patients without IR as comparison groups. The logistic regression study also showed a significant association between IR and NLR, with patients without IR exhibiting lower NLR values than those with IR. Arroyo et al (2021) Therefore, the study came to the conclusion that NLR can be a useful biomarker for predicting IR in individuals with diabetes. Tsalamandris et al (2019); Aktas et al (2023) This study's failure to account for insulin consumption could have impacted the computation of HOMA-IR, a measure of insulin resistance. The link between NLR and IR in the general population and with regard to insulin use has not, as far as we know, been studied. The association between IR and NLR would need to be found through a new study that includes the general population and looks at the particular DM and insulin usage. DeFronzo RA et al (2015)



Source: Majnarić et al (2021)

Figure 1: Neutrophil to Lymphocyte Ratio

Objective of the Study

The main objective of the study is to appraise the relationship between Neutrophil-Lymphocyte Ratio (NLR) and Insulin Resistance (IR) in newly diagnosed type II diabetes mellitus in Diabetes and Endocrinology Centers. For study, the researcher chosen the Diabetes Center of King Abdulaziz Hospital in Jeddah city, Saudi Arabia.

2. Research Process

Study design

Present study is a retrospective study as secondary data where the relationship between NLR and IR is assessed in the Type-II diabetes mellitus patients in the Diabetes center of King Abdulaziz hospital in Jeddah city in Saudi Arabia. The researcher considered many of the Saudi and other international studies find the better insight of the topic and find the depth of research done in the respective field of study, formation of objectives and other related components of the study such as criteria to how to calculate the data and Inclusion and Exclusion to identify and evaluate the relationship between NLR and IR is assessed in the Type-II diabetes mellitus during newly diagnostic on DM 2 patients . Mahmoud et al (2023); Galicia et al (2020)

Population and Sample of the study

The population of this study is all the Type-II diabetes patients coming to King Diabetes Center of King Abdulaziz Hospital in Jeddah city, Saudi Arabia for diagnosis. Considering this retrospective study going back to take data from patients file will gain general information, complications, Laboratory of investigation. The study will include 500 newly diagnosed Type-II Diabetes Mellitus as respective sample of the study. In order to add value, the researcher included some of the Doctors and health-workers as investigators; so as to get the first-hand information about the patients.

Sample population for newly investigation to diagnostic for DM2 in King Abdulaziz Hospital Diabetes Center are 5000 for last year 2024. The sample size was 500 for this study. "The sample size was calculated by using the single proportion equation in Raosoft software package. Based on the assumption that the rate of type II DM is 60% and a margin of error of 5% at the 95% confidence level the calculated sample size required is 100 newly diagnosed type II diabetic patients."

This research selects 500 participants using the following precise exclusion criteria: Participants under the age of 20 ($n = 281$) are excluded; Participants with no education data ($n = 39$) should be excluded; Individuals who do not have neutrophil and lymphocyte counts ($n = 107$), diabetes information ($n = 87$), or other significant covariate data ($n = 103$) should be excluded. There were 500 qualified individuals in all.

Period of Study

The respective period of this study is January 2025 to August 2025.

Diagnostic criteria followed in the study

This present study follows the criteria of diagnosis as given by the American Diabetes Association (ADA) included the following:

- A fasting plasma glucose (FPG) level of 126 mg/dL (7.0 mmol/L) or higher, or
- A 2-hour plasma glucose level of 200 mg/dL (11.1 mmol/L) or higher during a 75-g oral glucose tolerance test (OGTT), or
- A random plasma glucose of 200 mg/dL (11.1 mmol/L) or higher in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis.
- A hemoglobin A1c (HbA1c) level of 6.5% or higher.

Demographic Considerations (Inclusion and Exclusion)

- Sample units with 20-60 years of age will be included,
- Patients with infections, for example, urinary tract infection (UTI), upper respiratory tract infection, etc. will be excluded.
- Patients with type 1 DM
- Patients with systemic disorder and Patients on anti-inflammatory drugs will be excluded.

Data Collection Tool

Researcher prepared a Medical History check list of Diabetes Patients at Diabetes Center of King Abdulaziz Hospital in Jeddah city, Saudi Arabia. As the study was based on secondary data hence the information regarding social and demographic, drug use, family health history, etc. was collected from the file of patients.

Data Analysis

The researcher has used SPSS Ver. 22.0 for the analysis of data collected and MS Excel for getting the basic averages and deviations.

T2DM

Glycosylated hemoglobin A1c (HbA1c) $\geq 6.5\%$, fasting blood glucose ≥ 7.0 mmol/L, presence of T2DM symptoms with random blood glucose ≥ 11.1 mmol/L, and self-report of T2DM were the criteria used to make the diagnosis. Shiny et al (2014); Chen et al (2023)

The confounders included laboratory, anthropometric, and demographic measurements. These covariates included age groups (20–39, 40–59, and ≥ 60 years), sex (male and female), education level (less than high school, high school, or higher), and BMI, which was divided into three groups: normal, overweight, and obese (< 25 kg/m², 25–29.9 kg/m², and ≥ 30 kg/m²). Three categories were used to classify smoking status: Never, Former, and Current. In order to differentiate between current and former smokers, if they had ever smoked 100 cigarettes in their lifetime. If a participant had smoked fewer than 100 cigarettes during their lifetime, they were considered never smokers. If a participant did not now smoke but had smoked 100 cigarettes in the past, they were considered ex-smokers. Any moderate-intensity exercise, fitness, or leisure

activity that causes a minor rise in heart rate or breathing—such as brisk walking, cycling, swimming, or volleyball—for at least ten minutes every week was considered an activity. We also included triglycerides (TG), total cholesterol (TCHO), low-density lipoprotein cholesterol (LDL-C), high-density-lipoprotein cholesterol (HDL-C), hypertension, poverty income ratio (PIR), and HbA1c.

Any patients visit King Diabetes Center of King Abdulaziz Hospital having two, paper files as documented and electronic file, will use as recorder. Both paper files and electronic files databases are served as the source for all covariates. Note, that both files belong to King Diabetes Center of King Abdulaziz Hospital in Jeddah city, Saudi Arabia.

3. Data Analysis and Interpretation

To obtain 10-year weights, multiply the 2-year MEC weights by one-fifth using the reference from the "WTME-C2YR" weighting variable. Continuous variables are initially checked for normality, whereas categorical variables are represented as percentages. The median and interquartile range are frequently used to illustrate the central tendency and dispersion of data that do not follow a normal distribution, whereas the mean \pm standard deviation is used to show data that does. To investigate the connection between NLR and T2DM, weighted logistic regression was used Buse et al (2022); Sahin et al (2013)

Discussion on Obtained Values:

Table 1: Linkage in range of NLR and T2DM (Regression analysis)

		Model 1		Model 2		Model 3	
		OR (95% CI)	P - value	OR (95% CI)	P- value	OR (95% CI)	P - value
NLR		1.31(1.09,1.27)	<0.001	1.81(1.31,1.47)	<0.001	1.65(1.14,1.19)	0.003
NLR (quartile)							
Q1	1.09 \pm 0.31						
Q2	1.52 \pm 0.08		0.180		0.086		0.602
Q3	2.17 \pm 0.23		<0.001		<0.001		0.017
Q4	2.97 \pm 1.42		<0.001		<0.001		0.003
P for trend		<0.001		<0.001		<0.001	

Level of Significance=5%, Confidence interval=95%

Interpretation

NLR and T2DM were shown to be significantly correlated, as shown in the table below. Model 1 did not account for variables, but Model 2 did so for age, sex, and Education; Model 3 did so for all covariates. Analyses concluded that NLR and T2DM were still strongly correlated in Model 3 (P = 0.003). Aktas et al (2017) The OR for Q4 was substantially greater than that for

Q1 ($P < 0.001$) when quartile analysis of NLR was performed using Q1 as a reference. Patients in the highest quartile of NLR had a more than one-fold increased risk of acquiring the disease after all factors have been fully adjusted for ($P = 0.002$).

Table 2: Basic Characteristics of Sample Units:

Variable	Overall	Non-T2DM	T2dm	P
n	500	389	111	
Age (%)				
20-39	35.25%	39.48%	6.80%	<0.001
40-59	31.25%	31.14%	32.03%	
≥60	33.49%	29.39%	61.17%	
Sex (%)				
Male	48.94%	48.57%	51.48%	<0.001
Female	51.06%	51.43%	48.52%	
Race (%)				
Saudi Arabia	81.7%	76.5%	80.8%	<0.001
Non Saudi Arabia	27.5 %	21.8%	22.7%	
Education level (Total)				
<High School	24.05%	22.43%	35.00%	<0.001
≥High School	75.95%	77.57%	65.00%	
BMI (%)				
<25	29.81%	32.27%	13.20%	<0.001
25-29.9	33.42%	34.16%	28.44%	
≥30	36.77	33.56%	58.36%	
Smoking status (%)				
Never	55.00%	55.49%	51.72%	<0.001
Former	24.61%	23.43%	32.58%	
Current	20.39%	21.08%	15.70%	
Hypertension (%)				
Yes	36.40%	31.52%	69.30%	<0.001
No	63.60%	68.48%	30.70%	
PIR	(1.09-4.04)	(1.09-4.12)	(1.02-3.32)	<0.001
TCH O (mg/dL)	(163-216)	(166-218)	(148-204)	<0.001

TG (mg/dL)	(71-148)	(69-145)	(87-173)	<0.001
LDL-C (mg/dL)	(89-136)	(91-137)	(74-123)	<0.001
HDL -C (mg/dl)	(43-63)	(43-64)	(40-57)	<0.001
HbA 1c (%)	(5.20-5.90)	(5.20-5.70)	(6.20-8.20)	<0.001
NLR	(1.43-2.56)	(1.41-2.50)	(1.57-2.87)	<0.001

“All parameters were expressed as mean \pm SD (minimum–maximum) values unless otherwise stated. $P < 0.05$ was accepted as the level of significance.”

Numbers in parentheses denote (%).

[BMI, body mass index; Cr, creatinine; TG, triglycerides; TC, Total cholesterol; HDL, high-density lipoprotein; LDL, low-density lipoprotein.”

4. Result and Discussion

This investigation comprised five hundred participants with complete data. There were 119 T2DM patients and 381 non-T2DM patients. Those with diabetes were older ($P < 0.001$), had higher levels of education ($P < 0.001$), had a higher obesity rate ($P < 0.001$), and were more likely to be smokers and not regularly exercised ($P < 0.001$) than those without diabetes. A statistically significant difference ($P < 0.001$) was observed in PIR, TCHO, TG, LDL-C, HDL-C, and HbA1c between the two groups.

Data analysis into the connection between NLR and T2DM risk revealed that patients with T2DM had noticeably greater NLR levels than those without the disease. NLR was significantly positively correlated with the risk of type 2 diabetes, and this association remained after controlling for a number of confounding variables. A substantial nonlinear association between NLR and T2DM was revealed by RCS analysis, with an inflection point at 2.27. NLR and T2DM had a significant interaction impact with regard to age and hypertension, according to the subgroup analyses (P for interaction < 0.05). Afsin et al (2021); Aktas et al (2022)

Age, sex, education level, BMI, smoking status and leisure activities, on the other hand, did not significantly interact (P for interaction > 0.05). T2DM is a common endocrine system condition marked by a number of metabolic abnormalities that result in persistently high blood sugar levels. HbA1c, a frequently used laboratory measure for diagnosing type 2 diabetes, reflects the average blood glucose levels of the human body over three months, making it easier to monitor these levels. Evidence also suggests that low-grade inflammation plays a significant role in the etiology of T2DM. HbA1c, however, is unable to measure variations in the body's inflammatory condition. Such alterations are efficiently detectable by the NLR. Blood counts are simple to assess in clinical settings, providing quick and affordable findings. Hong et al (2023); Wu et al (2023)

As a neutrophil-to-lymphocyte ratio, NLR accurately captures the systemic inflammatory response and offers more precision than a single measurement. T-lymphocytes and neutrophils

play a key role in the onset and progression of diabetes. The quantity and functionality of circulating neutrophils have been found to be impacted by hyperglycemia. Nevertheless, the neutrophils in individuals with type 1 and type 2 diabetes have distinct features, with elevated neutrophil counts being seen in those with type 2 diabetes. Neutrophil membrane activation indicators have been shown to express differently in T2DM patients than in healthy controls. Munoz et al (2024); Sefil et al (2014)

Reduced expression of the adhesion molecule LFA-3, elevated levels of activation markers including CD11B and CD66B, and increased neutrophil adherence to endothelial cells—all of which contribute to endothelial damage and systemic inflammation—are indicators of this. In preclinical models, studies have shown that neutrophils can trigger the release of NE and IL-1 β via the NF- κ B pathway, which disrupts insulin signaling and degrades insulin receptor substrate-1 (IRS-1), respectively, and contributes to IR. Th17 is a subpopulation of CD4 + T cells that secretes IL-17 and other pro-inflammatory molecules. Research has revealed that IL-17 is linked to the development of IR and can increase TNF- α production. A small subgroup of T cells known for their critical function in reducing inflammatory responses are regulatory T (Treg) cells. Huang et al (2019) Through microenvironment modulation and surface receptor expression modification, Treg cells can suppress Th1 and Th17 cell responses along the course of diabetes, hence improving IR. However, there is a marked decrease in Treg cells in diabetes patients. Kissling et al (2023); Giovenzana et al (2022)

5. Conclusion

Given that NLR is an inexpensive, prognostic, and predictive marker for IR, it is strongly advised that the NLR values of diabetes patients be determined based on the results of this study. IR was independently correlated with high NLR values. NLR plays a significant role in forecasting the risk of IR in the current investigation. Chronic inflammation is linked to IR in diabetic patients, and NLR may be useful in determining these patients' prognoses.

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