



Is There a Relationship between Insulin Resistance and Eosinophil, Inflammatory Parameters Neutrophil to lymphocyte ratio, C-Reactive Protein Values?

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Abstract

Aim: The relationship between insulin resistance and inflammation and atopy is a matter of curiosity and various studies have been conducted. Study results show differences. We aimed to evaluate the relationship between insulin resistance and inflammation and atopy using C-Reactive Protein (CRP) and Neutrophil to lymphocyte ratio (NLR) as eosinophils and inflammatory indices and to determine whether the low-cost hemogram can be used as a reliable marker.

Material and Method: Between May 2022 and November 2023, 1566 children admitted to the Pediatrics outpatient clinics of İzmir Bakırçay University Çiğli Training and Research Hospital were retrospectively screened. A total of 349 pediatric patients without any known chronic disease and with complete blood count, CRP and HOMA-IR levels were retrospectively included in the study.

Results: Individuals with HOMA-IR<2.5 were considered as control group and those with HOMA-IR≥2.5 were considered as children with insulin resistance. As a result of Mann-Whitney-U test performed according to HOMA-IR groups, age and NLR parameters were found to be higher in the group with insulin resistance. This result was statistically significant ($p<0.05$). The results were not significant in eosinophil ($p=0.324$) and CRP ($p=0.352$) parameters.

Conclusion: NLR value may be a credible predictive marker of insulin resistance. Inexpensive and simple complete blood count measurement may help in the early diagnosis of Type 2 DM and in the design of treatments. In addition, due to the increasing risk of insulin resistance with age, education on conscious nutrition can be given in schools during adolescence.

Keywords: Neutrophil-to-lymphocyte ratio, Insulin resistance, Inflammation, eosinophils, CRP

INTRODUCTION

Obesity has become an increasingly common health problem in both children and adults (1,2). The HOMA-IR value is an important tool for detecting and measuring insulin resistance (IR) indicator. Obesity and IR are often directly proportional. Obesity in general is a health problem that negatively affects the whole system and even leads to metabolic consequences.

IR is known to be one of the main causes of Diabetes Mellitus Type 2 (T2DM), but the mechanism of IR is not fully understood. Some studies have shown that there may be an association between IR and inflammation (3,4). IR may trigger allergic diseases and inflammation through

different mechanisms. In individuals with high IR, plasma IL-6 level was found to be high, which also increased in inflammation (5).

Eosinophils are immune cells associated with parasitic infections and allergic reactions. They are produced from multipotent hematopoietic stem cells in the bone marrow. They are involved in the pathology of chronic inflammation directly or by producing inflammatory cytokines (6).

The prevalence of both obesity and asthma has increased rapidly in recent years and the association of these two diseases is remarkably high. Although some studies have shown that aeroallergen sensitization is higher in obese children, no clear information has been found. Mechanisms

CITATION

Yigit M, Olukman O. Is There a Relationship Between Insulin Resistance and Eosinophil, Inflammatory Parameters Neutrophil to lymphocyte ratio, C-Reactive Protein Values?. Med Records. 2024;6(1):32-6. DOI:1037990/medr.1398279

Received: 30.11.2023 **Accepted:** 22.12.2023 **Published:** 10.01.2024

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that may explain this relationship include increased chest wall weight and/or reduced lung volumes due to pro-inflammatory mediators released by adipocytes (7,8).

NLR is a recently popular and frequently used parameter in subclinical inflammation. It is calculated by the ratio of neutrophil and lymphocyte percentages in hemogram analysis (9,10). Increased neutrophil to lymphocyte ratio as a result of increased neutrophil count and decreased lymphocyte count is considered as an indicator of immune response and inflammation. NLR is also used to measure the severity of the disease (11). NLR has become an inexpensive and reliable method used to determine both cardiac and non-cardiac inflammation (11,12). More studies needed to understand the relationship between IR and NLR.

CRP is a protein that indicates tissue damage and inflammation and is produced by the liver. CRP measurement, which is used as an inflammatory marker, is a simple and inexpensive test.

Some studies have shown that IL-6, TNF-alpha and CRP levels are higher in obese patients, but the number of studies is not sufficient and more studies are needed. In a study by Park et al. it was reported that there was a direct relationship between CRP and body mass index and between IL-6 and body fat ratio (14).

In this study, we tried to determine the relationship of peripheral eosinophil percentage with IR and whether elevated inflammatory indices suggest IR by using a simple and inexpensive test of complete blood count and CRP measurement.

MATERIAL AND METHOD

Study Population and Design

The study was conducted with the decision of the Local Non-interventional Ethics Committee 1233 dated 11.10.2023. It was conducted in the pediatrics department of a training and research hospital. In the study, 1566 children aged 3-17 years were retrospectively screened and 349 children with complete blood count, CRP and HOMA-IR tests and without known chronic diseases were included in the study. As a result, the study was conducted on 160 males and 189 pediatric subjects. The

blood findings of the individuals were retrospectively selected randomly from the hospital archive system and those with HOMA-IR level <2.5 were selected as control group and those with HOMA-IR level \geq 2.5 were selected as insulin resistant group. Eosinophil, CRP and NLR values were also included in the study. Demographic information of the individuals was also recorded. Children with a history of chronic disease were excluded from the study as exclusion criteria.

Statistical Analysis

The conformity of the data to normal distribution was tested with the Anderson Darling test, which is a normality test. Median, minimum and maximum values were included in the descriptive statistics of the data. Mann Whitney-U test was used for analysis between two groups. The relationship between the data was revealed by Spearman rho correlation analysis and the level of HOMA-IR determination of the parameters was revealed by ROC analysis. SPSS 21 package program was used for statistical analysis with $p < 0.05$.

RESULTS

As a result of the normality test, it was found that all parameters did not show normal distribution according to HOMA-IR groups ($p \geq 0.05$). Descriptive statistics of the control and insulin resistant groups are given in Table 1.

As a result of Mann-Whitney-U test, age, NLR and HOMA-IR parameters were found to be significantly different between insulin groups ($p < 0.05$). There was no significant difference in eosinophil ($p = 0.324$) and CRP ($p = 0.352$) parameters.

The relationship between the parameters and the degree of relationship were evaluated by Spearman rho correlation test and a moderate significant relationship was found between HOMA-IR and age. Very weak correlations were found between CRP and eosinophils, NLR and age, eosinophils and CRP, and HOMA-IR and NLR (Table 2).

The effect of the parameters was evaluated by ROC analysis and it was found that the age parameter had the highest effect, followed by the NLR parameter (Figure 1, Table 3).

Table 1. Descriptive statistics according to insulin groups

Parameters	Group	Minimum	Median	Maximum
Age	Control	3.00	7.00	17.00
	IR	3.00	13.00	17.00
Eosinophil	Control	0.00	2.60	40.00
	IR	0.10	2.40	13.00
CRP	Control	0.30	0.56	207.00
	IR	0.30	0.66	45.00
NLR	Control	0.34	1.07	26.00
	IR	0.47	1.46	12.15
HOMA-IR	Control	0.10	0.90	2.40
	IR	2.50	3.95	17.00

Table 2. Spearman rho correlation table

Parameters	Age	Eosinophil	CRP	NLR
Eosinophil	-0.088			
	0.102			
CRP	-0.037	-0.138		
	0.486	0.010		
NLR	0.331	-0.230	0.227	
	0.000	0.000	0.000	
HOMA-IR	0.636	-0.008	-0.010	0.281
	0.000	0.878	0.849	0.000

Table 3. ROC performances

Parameters	AUC (95%)	Cutt off	p	Sensitivity	Specificity
Gender	0.452 (0.392-0.513)	1.50	0.124	49	41
Age	0.821 (0.777-0.865)	10.50	0.000	73	76
Eosinophil	0.472 (0.411-0.533)	2.55	0.369	47	49
CRP	0.529 (0.468-0.590)	0.58	0.352	53	53
NLR	0.647 (0.589-0.705)	1.293	0.000	63	63

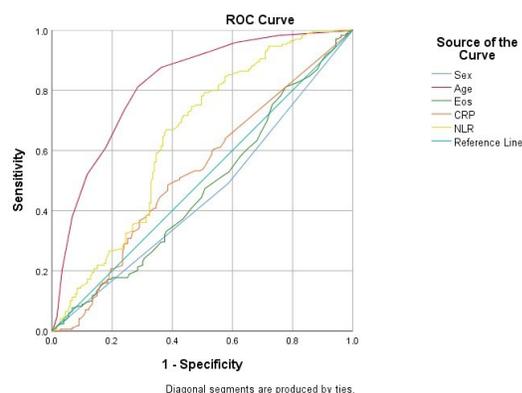


Figure 1. ROC Curve

DISCUSSION

Eosinophils are produced from multipotent hematopoietic stem cells in the bone marrow. Immune cells, including eosinophils, play a role in the pathology of chronic inflammation, either directly or by producing inflammatory cytokines (6).

There are some studies investigating the effects of asthma, atopy and insulin resistance. However, these studies have shown inconsistent results.

Lee et al. found a significant association between insulin resistance and total IgE in premenopausal women, but not in men or postmenopausal women (15).

In a Danish study, IR was directly associated with asthma-like symptoms (16). In a study by Ma et al. on adults in the USA, insulin resistance has not been found to be a risk factor for allergies (17). In a study by Zhu et al. on 9111 Chinese adults, the percentage of eosinophils was inversely correlated with the risk of T2DM (18). In another study conducted in the United States, the association between IR and asthma was found to be significant (19).

The differences between these results were thought to be due to differences in the study population. In our study, no significant association was found between eosinophil percentage and IR.

There is chronic inflammation in the mechanism of many diseases, however, many studies have shown that chronic inflammation is involved in the pathogenesis of T2DM. This suggests that IR and inflammation may be related and there may be a potential relationship between IR and inflammatory markers NLR and CRP. Inflammatory factors such as CRP, TNF- α , IL-6 and MCP-1 are elevated in patients with T2DM and this is thought to be due to chronic inflammation. Chronic inflammation results in high neutrophil counts (20). IR was significantly associated with increased NLR in the study by Lou et al. (21). In the study of Atli et al. CRP levels were found to be significantly higher in obese patients compared to non-obese patients, but no statistically significant difference was found in NLR and PLR values. (22). In a study by Karakaya et al. NLR was significantly higher in obese patients with IR was detected (23). In a study conducted by Sarıcam on 274 patients, the relationship between insulin resistance and inflammatory parameters was found to be significant (24).

In a study conducted by Gelaye et al. on Peruvian adults, a significant association between high insulin resistance and increased CRP was found (25). Kim et al. found a significant positive association between IR and elevated CRP in a study group with a sample of 36 patients in 2011 (26). In our study, no significant correlation was found between IR and CRP. However, a significant direct correlation was found between NLR and IR. Inflammatory markers such as CRP and NLR may be a helpful method for early diagnosis of T2DM, but more research is needed to confirm this observation.

The study by Yang et al. showed that IR increased with increasing age (27). In a study by Strazhesko et al. it

was shown that HOMA-IR was inversely associated with telomere length (28). Because of the shortening telomere length with increasing age and the inverse relationship between IR and telomeres, this resulted in a direct relationship between age and IR. This suggests that the probability of increasing IR increases with increasing age. However, more studies are needed on this subject. In our study, a significant relationship was found between IR and age. The probability of IR increased with increasing age.

CONCLUSION

High NLR value may be a suitable predictive marker of IR. However, more studies are needed because of different results in the studies on the relationship between CRP and eosinophil percentage and IR. Detection of an elevated NLR value by complete blood count measurement, which is a simple and inexpensive test, may help in the early diagnosis of T2DM. Due to the significant direct correlation between IR and age, proper nutrition education and counseling is especially important during adolescence.

Financial disclosures: The authors declared that this study has received no financial support.

Conflict of interest: The authors have no conflicts of interest to declare.

Ethical approval: Ethical approval was obtained from İzmir Bakırçay University Faculty of Medicine (decision no: 133 research no: 1213 date: 11.10.2023).

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