

# Neutrophil to lymphocyte ratio in patients with vitiligo

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## Abstract

**Introduction:** There are a few studies showing an increased risk of insulin resistance, metabolic syndrome, and oxidative stress in patients with vitiligo.

**Aim:** To investigate whether systemic inflammation is increased in vitiligo patients in a case-control study design.

**Material and methods:** Nonsegmental vitiligo patients who had been followed at the outpatient dermatology clinic of a university-affiliated teaching hospital, and healthy controls were enrolled in the study. Patients who were receiving systemic treatments and having a systemic disease such as diabetes mellitus and thyroiditis were excluded. Demographic features were recorded and peripheral blood samples were taken from all participants to study serum whole blood count, creatinine, and C-reactive protein (CRP).

**Results:** Fifty patients with localized vitiligo, 43 patients with generalized vitiligo, and 50 healthy volunteers were enrolled in the study. Neutrophil to lymphocyte ratio and serum CRP levels were significantly higher in patients who have generalized vitiligo than those with localized vitiligo and healthy controls. However, there was no significant difference regarding neutrophil to lymphocyte ratio (NLR) and CRP between localized vitiligo and control groups.

**Conclusions:** Patients with generalized vitiligo seem to have increased systemic inflammation compared with localized vitiligo and control subjects in our cohort. To the best of our knowledge, this is the first study in the literature showing increased NLR values in generalized vitiligo patients. Further studies with cardiovascular disease markers are required to elicit this association better.

**Key words:** neutrophil to lymphocyte ratio, vitiligo, inflammation.

## Introduction

Vitiligo is a pigmentary disorder affecting 0.5–1% of the general population. Though several hypotheses such as genetic tendency, autoimmune, neuro-humoral, auto-cytotoxic, and oxidative stress hypothesis have been proposed in pathophysiology of vitiligo, the exact etiology of vitiligo is unknown [1]. Although formerly it is thought that vitiligo is a disease which is only limited to the skin, recently some studies showed an increased frequency of insulin resistance, and metabolic syndrome in patients with vitiligo [2–4].

Neutrophil to lymphocyte ratio (NLR) is a novel inflammatory parameter and can be easily calculated from the differential of a complete blood count result. It has been shown that NLR is independently associated with cardiovascular morbidity and mortality [5]. To the best of our knowledge, data are scarce in the literature regarding increased systemic inflammation in vitiligo patients.

## Aim

Thus, we aimed to evaluate the presence of systemic inflammation in a cohort of vitiligo patients in a case-control study design.

## Material and methods

This was a case-control study which was conducted at the outpatient dermatology clinic of a university-affiliated teaching hospital. Patients who were receiving systemic treatments (corticosteroids and other drugs which have the potential to affect NLR), and had systemic diseases such as diabetes mellitus were excluded. One hundred consecutive nonsegmental vitiligo patients who had vitiligo for at least 6 months were screened for eligibility for study inclusion. Fifty healthy volunteers to serve as the control group were included in the study. Four patients were excluded from the study since they did not give blood samples for biochemical analysis, and

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3 patients due to accompanying diabetes mellitus and autoimmune thyroiditis. Finally, 93 patients with nonsegmental vitiligo were included in the study. Demographic characteristics were recorded for all participants. Peripheral blood samples were collected from all study participants to study complete blood counts and differential, serum creatinine, and C-reactive protein (CRP).

Neutrophil to lymphocyte ratio was calculated from complete blood counts as the ratio of peripheral blood neutrophil count to lymphocyte count. An estimated glomerular filtration rate (eGFR) was calculated by using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [6].

### Statistical analysis

Analyses were performed using statistical software (IBM SPSS Statistics 20, SPSS Inc. an IBM Corp., Armonk, NY). One-way ANOVA test was used to compare normally distributed variables in three groups. Post-hoc Bonferroni correction was used for comparing numeric variables between three groups.

Normally distributed variables were presented as mean  $\pm$  standard deviation. *P*-value of  $< 0.05$  was deemed as statistically significant.

### Results

Ninety-three patients with nonsegmental vitiligo (50 patients with localized vitiligo, and 43 patients with generalized vitiligo) and 50 healthy volunteers were enrolled in the study. Comparison of the demographics and laboratory results of localized and generalized vitiligo and control groups are shown in Table 1. The NLR values and serum CRP levels were significantly higher in patients who have generalized vitiligo than those with localized vitiligo and healthy controls. There was no significant difference regarding NLR and CRP between localized vitiligo group and controls.

There was no significant difference regarding eGFR between the patients with vitiligo and controls. There were no patients with eGFR values below 90 ml/min/1.73 m<sup>2</sup>.

### Discussion

The salient finding of this study was that neutrophil to lymphocyte ratio and serum C-reactive protein levels were significantly higher in patients who have generalized vitiligo compared with patients who have localized vitiligo and healthy controls. However, there was no significant difference regarding NLR and CRP between the localized vitiligo group and controls. Generalized vitiligo seemed to be associated with increased systemic inflammation. And for the first time in the literature, our results showed increased NLR values in generalized vitiligo patients.

It has been shown that melanocytes are present in adipose tissue as well as the skin, eye, inner ear, and leptomeninges [4, 7, 8]. The melanocytes in the adipose tissue are believed to exert anti-inflammatory actions and have a role in reduction of reactive oxygen species (ROS) [8, 9]. The clinical importance of this observation arises from the fact that a decrease in the number of melanocytes and reduced melanogenesis in the adipose tissue may lead to metabolic disturbance in vitiligo patients since oxidative stress plays a role in the pathogenesis of metabolic syndrome [7, 10, 11].

Tu *et al.* [12] demonstrated that serum IL-6 and granulocyte-macrophage colony-stimulating factor (GM-CSF) levels were significantly higher in vitiligo patients with both focal type and generalized type than those of controls, and the serum IL-1 $\beta$  level was also higher in vitiligo patients with a generalized type compared to controls. Similarly, it has been shown that nonsegmental vitiligo patients had increased levels of interferon- $\gamma$  (IFN- $\gamma$ ) but decreased levels of interleukin-10 (IL-10) compared to controls. As IFN- $\gamma$  is a pro-inflammatory and IL-10 is an anti-inflammatory cytokine, the results of the latter study support that inflammation may be increased in patients with vitiligo [13]. However, in another study, it has been shown that patients with vitiligo have a better lipid profile than controls. Therefore, the authors suggested that vitiligo patients might have a lower cardiovascular risk. But they did not mention about the severity or type of vitiligo, be it focal or generalized, in their study cohort [14].

**Table 1.** Comparison of the demographic features and laboratory results of localized and generalized vitiligo and control groups

Parameter	Localized vitiligo group (n = 50)	Generalized vitiligo group (n = 43)	Controls (n = 50)	P-value
Gender:				
Female	25 (50%)	20 (46.5%)	25 (50%)	0.929
Male	25 (50%)	23 (53.5%)	25 (50%)	
Age	37.6 $\pm$ 12.1	42.3 $\pm$ 15.0	42.4 $\pm$ 10.1	0.092
eGFR [ml/min/1.73 m <sup>2</sup> ]	109.3 $\pm$ 13.5	103.9 $\pm$ 19.9	105.3 $\pm$ 12.2	0.206
NLR	1.64 $\pm$ 0.48	2.09 $\pm$ 0.86	1.69 $\pm$ 0.46	0.001
CRP [mg/l]	3.03 $\pm$ 1.98	3.99 $\pm$ 2.47	2.78 $\pm$ 1.02	0.007

eGFR – estimated glomerular filtration rate, NLR – neutrophil to lymphocyte ratio, CRP – C-reactive protein.

None of the aforementioned studies except one provided data regarding extensity of the vitiligo. According to results of our study, generalized type vitiligo, but not localized type, is associated with high systemic inflammation, which corroborates the hypothesis that vitiligo may be a systemic disease [4]. In addition, since high NLR was shown to be associated with an increased risk of metabolic syndrome, and cardiovascular disease, our results indirectly lend support to the observation that cardiovascular disease in vitiligo patients may be increased owing to increased systemic inflammation [2–5, 15].

The NLR is a novel inflammatory marker which has been associated with increased clinical adverse outcomes in several patient populations independent of traditional cardiovascular risk factors [16, 17]. Thus, in our opinion, increased NLR may be an important risk factor for cardiovascular disease in these patients.

We took eGFR values into account when evaluating NLR values in patients and controls because of the fact that reduced GFR may increase NLR values per se [5]. There was no patient with chronic kidney disease in our cohort, so we could control the confounding effect of eGFR on NLR values.

There are some limitations in our study that deserve to be mentioned. First, the sample size was relatively small. Second, it would be better to evaluate patients clinically in terms of established cardiovascular disease markers such as carotid intima media thickness. Nevertheless, this is the first study assessing NLR, a novel inflammatory parameter, in vitiligo patients. More importantly, our study is the preliminary one showing that extent of vitiligo might be associated with the degree of systemic inflammation.

## Conclusions

Patients with generalized vitiligo seem to have increased systemic inflammation in our cohort. This systemic inflammation may be one of the putative missing links between an increased cardiovascular and metabolic risk in vitiligo patients. However, further studies are needed to extend our findings in larger cohorts and link increased inflammation with cardiovascular disease markers.

## Conflict of interest

The authors declare no conflict of interest.

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