

# Inflammatory and infectious parameters in tension-type headache

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## Abstract

Although tension-type headache (TTH) is the most common primary headache in the world, much fewer studies on its pathophysiology have been carried out in comparison to other primary headaches. Inflammatory processes are important in the pathophysiology of both peripheral and central pain. Studies on the role of inflammatory markers in TTH patients are limited. Therefore, in this study, it was aimed to examine the role of inflammatory parameters in TTH. 199 TTH patients and 154 control participants were involved in this study. C-reactive protein (CRP) and high-density lipoprotein (HDL) levels and neutrophil/lymphocyte (NLR), platelet/lymphocyte (PLR), monocyte/lymphocyte (MLR), HDL/monocyte and Immature/Total granulocyte ratios in all patients reviewed retrospectively. CRP value and immature/total granulocyte ratio were found to be significantly higher in the patient group when compared to the control group. No difference was found between NLR, PLR, MLR, and HDL/Monocyte ratios. There was no difference in NLR, MLR, immature/mature granulocyte ratios, and CRP values between the genders in the patient group. Median values of PLR, HDL, and HDL / monocyte were found to be higher in males. The fact that there is no difference in most of the inflammatory parameters in TTH and there is a significant difference in the immature/total granulocyte ratio is a new finding on this subject. There is no other study in the literature examining the immature/total granulocyte ratio in headaches.

**Keywords:** Neutrophil / lymphocyte ratio, platelet / lymphocyte ratio, immature / mature granulocyte ratio, tension-type headache

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## Introduction

Even though tension-type headache (TTH) is the most common primary headache around the world, there are much fewer studies examining its pathophysiology when compared to other primary headaches. Although it is thought that genetic and environmental factors play a role together in its pathogenesis [1], the factors causing the attacks couldn't be clearly revealed yet. In recent years, it was claimed that the changes in both peripheral and central pain pathways played a role in pathophysiology [1,2]. The number of studies examining the role of inflammatory indicators in tension-type headache patients is limited. It was reported in the literature that some inflammatory indicators, which can be easily achieved from complete blood analyses, could be used in many diseases [2,4].

The present study aims to investigate the roles of neutrophil / lymphocyte (NLR), platelet / lymphocyte (PLR), monocyte / lymphocyte (MLR), HDL / monocyte, and immature / total granulocyte ratios and CRP values in tension-type headache.

## Materials and Methods

In the present study, examining the files of patients aged 18 years or older who were followed and tested for headaches in the Neurology Department Polyclinic of the Medical Faculty of Sanko University and diagnosed with a tension-type headache by using the International Classification of Headache Disorders-III [5], complete blood, CRP, and HDL values were recorded. The control group who applied to our hospital for general medical examination, have no neurological disease or primary headache history known and were not diagnosed with any neurological disease during the neurological analyses and tests. For all cases, monocyte / lymphocyte ratio (MLR) is calculated by dividing monocyte and lymphocyte counts, neutrophil / lymphocyte ratio (NLR) is calculated by dividing neutrophil and lymphocyte counts, platelet / lymphocyte ratio (PLR) is calculated by dividing platelet and lymphocyte counts, monocyte / HDL ratio calculated by dividing monocyte and HDL values, and immature / total granulocyte ratio is calculated by dividing immature and total granulocyte counts were

statistically compared.

The present study was carried out in accordance with the principles of the Helsinki Declaration. Ethics committee approval was obtained from the Ethics Committee of the Medical Faculty of Sanko University on 2022/2.

## Statistical Analysis

The data were analyzed using IBM SPSS V23. Fitness to normal distribution was tested using the *Kolmogorov-Smirnov* test. Comparison of categorical data by the groups was performed using the Chi-Square test. Comparison of non-normally distributed data by paired groups was performed using the *Mann Whitney-U* test, whereas samples *t*-test was used in comparing the normally distributed data. Statistical significance was set at  $p < 0.050$ . In this study, the minimum sample size was found to be 102 when the sample size was calculated as  $\alpha = 0.05$  and  $\text{power} = 0.80$  with 1 unit deviation.

## Results

In the present study, 199 TTH patients having the mean age of 46.4 years (81 male patients) and 154 control cases having the mean age of 44 years (74 male participants) were involved. There was no statistically significant difference between the groups in terms of age and gender distribution ( $p = 0.380$  and  $p = 0.168$ , respectively). There was no statistically significant difference between the patient and control groups in terms of NLR, PLR, MLR, and HDL / monocyte ratios but there was a statistically significant difference between the groups in terms of CRP and immature / total granulocyte ratios ( $p = 0.026$  and  $p = 0.004$ , respectively) (Table 1). In the patient group, no statistically significant difference was found between the genders in terms of NLR, MLR, immature / total granulocyte ratios and CRP values. Considering the gender, PLR median value was found to be 108.7 among females and 118.4 among males; there was a statistically significant difference ( $p = 0.043$ ). By gender, HDL median value was found to be 47.0 among females and 50.0 among males; there was a statistically significant difference ( $p = 0.009$ ). HDL / Monocyte median value was found to be 0.080 among women and 0.090 among men and there was a statistically significant difference ( $p < 0.001$ ).

## Discussion

The number of studies examining TTH and peripheral inflammation is limited [6,7]. The effects of systemic inflammation on tension-type headache are not clearly known. Differing from migraine, in which the role of neuroinflammation via trigeminovascular activation is accepted, the pathophysiology of TTH couldn't be understood yet [8]. Since it was found in several previous studies that proinflammatory cytokines were found to be at high levels in serum and cerebrospinal fluid in TTH, it was thought that inflammatory parameters might be considered for TTH pathophysiology [8-11]. In the present study, CRP value and immature/total granulocyte ratio were found to be higher in the patient group but there was no difference between NLR, PLR, MLR, and HDL / Monocyte ratios.

In a previous study, it was determined that TTH patients' thrombocyte counts and NLR, PLR, and CRP values were statistically significantly higher [7]. There also are studies relating these ratios to migraine [12,13]. In studies carried out, especially during migraine attacks, it was found that NLR and PLR were higher than in the control group [12]. In the literature, there also

are studies reporting no significant difference between migraine patients and control groups in terms of NLR and PLR values [14].

Immature granulocytes were reported to be higher in peripheral blood mainly in diseases such as sepsis, acute infections, and acute appendicitis [15,16]. Immature granulocytes include metamyelocytes, myelocytes, and promyelocytes; they are precursors of neutrophils and they indicate increased bone marrow activity [17]. The immature/mature granulocyte ratio was reported to increase in some hematological and autoimmune diseases and be an important bioindicator [17,18]. Moreover, it was stated that it can be defined as both early diagnosis and prognosis bioindicator in sepsis and surgical diseases such as acute pancreatitis and acute appendicitis [15,19]. However, in the literature, there is no study examining this parameter in relation to headaches. Immature/mature granulocyte values have just started to be studied in our laboratory. So we wanted to investigate this as a biomarker for tension-type headache. In the present study, both immature and mature granulocyte counts were found to be higher in TTH patients in comparison to the control group. Moreover, a statistically

**Table 1.** Comparison between peripheral blood parameters in patient and control groups.

Groups	Patient (n=199)	Control (n=154)	<i>p</i>
	(min-max) mean	(min-max) mean	
HDL (mg/dl)	(12-113) 49	(25-85.) 48.5	0.809
CRP (mg/L)	(0.09-28.1) 2.46	(0.2-26.1) 1.8	0.026
NLO	(0.22-24.49) 1.9	(0.54-7.37) 1.77	0.058
PLO	(44.9-517.8) 113.8	(45.9-308.3) 116.3	0.954
MLO	(0.07-0.97) 0.24	(0.11-0.89) 0.25	0.986
HDL / Monocyte	(0.02-0.34) 0.09	(0.03-0.26) 0.09	0.75
Immature / Total granulocyte	(0-0.02) 0.003	(0-0.02) 0.002	0.004

significantly higher immature/total granulocyte ratio suggests that immature granulocytes were higher than the total in the patient group.

The strengths of this study are as follows; it is known that the participants in the control group had no neurological disease and / or pain syndrome and the numbers of cases in the patient and control groups were enough. However, the limitations are that complete blood counts of TTH patients were obtained retrospectively and the results were not compared to clinical characteristics such as duration, frequency, and severity of headache.

## Conclusion

In the present study, it is difficult to interpret the significantly higher immature / total granulocyte ratio by using the available data. To the best of our knowledge, there is no other study examining the immature / total granulocyte ratio in relation to headaches. In this study, the finding that patient and control groups were similar to each other in terms of NLR, PLR, and MLR values, which have been more widely studied in the literature, but different in terms of CRP and immature/total granulocyte ratio suggests that more useful information can be achieved from more detailed prospective studies examining clinical and laboratory data together.

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## Conflict of interest

The author declares no conflict of interest regarding this article.

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