

# Systemic Inflammatory Blood Markers In Patients With Tympanosclerosis

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## ABSTRACT

Tympanosclerosis is a disorder as known hyaline accumulation in the middle ear. Inflammation has been proposed in the development of tympanosclerosis. The mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR) and red cell distribution width (RDW) are most common markers of systemic inflammation.

Fourty patients who diagnosed tympanosclerosis intraoperatively and 35 subjects without tympanosclerosis were enrolled in this retrospective study. The MPV, RDW, neutrophil and lymphocyte as well as platelet counts were evaluated from complete blood counts in both trial participants. NLR was calculated.

The purpose of this research was to determine blood systemic inflammatory markers in patients with tympanosclerosis.

The average age of patients with tympanosclerosis was  $23.4 \pm 9.2$  years, and it was found  $24.7 \pm 8.9$  years in subjects without tympanosclerosis. There were 21 female and 19 male in subjects with tympanosclerosis and 17 female and 18 male in subjects without tympanosclerosis. Two groups have similar results with respect to age and gender. There was no important difference between two research participants with respect to the MPV, RDW and NLR ( $p > 0.05$ ).

We could not find any association between the markers of blood systemic inflammatory and tympanosclerosis. Therefore, tympanosclerosis does not seem to change the systemic inflammation.

**Key Words:** Otitis Media, Tympanosclerosis, Mean Platelet Volume, Red Cell Distribution Width, Neutrophil to Lymphocyte Ratio

## Introduction

Tympanosclerosis is a condition characterized by hyaline and calcified collagen accumulation in the submucosa of the middle ear. Various studies have reported the incidence of tympanosclerosis between 7 and 33% in some series of subjects with chronic otitis media (1). The exact pathophysiology of tympanosclerosis is well unclear. Up to now, several hypotheses have been mentioned to clarify the tympanosclerosis formation. Inflammation, middle ear infection, chemical agents, immunity and tympanic membrane trauma, such as myringotomy and ventilation tube insertion are reported as major factors of tympanosclerosis (2). Clinical and *in vivo* researches have elucidated that formation of oxygen radicals induced by bacteria and inflammatory cells in otitis media have a crucial role in the development of tympanosclerosis (3).

Some parameters routinely measured from the peripheral blood analysis have been popularized lately as inflammatory markers. The neutrophil-to-lymphocyte ratio (NLR) is described as an important indicator of systemic inflammation. NLR can routinely be used in peripheral blood without

additional cost (4). High NLR correlates with the severity of the inflammation (5). Another inflammatory marker, mean platelet volume (MPV) measurement is based on the size of the platelets in the peripheral blood. It is a readily available marker of platelet activation. The MPV is an indicator of increased platelet activity, and thus, more intense inflammation. During activation, the platelet size tends to increase, and thus, they become more reactive (6, 7).

Red cell distribution width (RDW) gives information about the variation in size of all the red blood cells (RBCs). The RDW is routinely provided within the complete blood count (CBC) done by automated analyzers. It is elevated when an excess of reticulocytes is released into the circulation. Over and above its role in the evaluation of anemia, RDW was shown to be a prognostic marker in the patients with cardiovascular disorders, pulmonary embolism, respiratory diseases and critical illness (8).

According to published data, there is no paper to investigate the association between tympanosclerosis and MPV, NLR and RDW. Therefore, the present study was designed to establish whether MPV, NLR and RDW are used as a systemic inflammatory marker

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Received: 23.05.2018, Accepted: 18.10.2018

**Table 1.** Demographic data of the subjects

	Subjects with Tympanosclerosis (n=40)	Subjects without Tympanosclerosis (n=35)	
Sex			
Female	21	17	ns
Male	19	18	
Age (years)	23.4±9.2	24.7±8.9	ns

ns: non significant

Values are mean ± SD;

**Table 2.** Blood systemic inflammatory markers in tympanoplasty performed subjects

	Subjects with Tympanosclerosis (n=40)	Subjects without Tympanosclerosis (n=35)	p
Mean Platelet Volume (fL)	8.52 ± 0.98	8.27 ± 0.91	0.268
Red Cell Distribution Width (%)	13.8 ± 1.43	13.5 ± 0.85	0.284
Neutrophil-to- Lymphocyte Ratio (%)	2.25 ± 1.10	2.09 ± 0.77	0.459

Values are mean ± SD;

of tympanosclerosis. In this context, this article is the first to study the link between tympanosclerosis and these blood markers which is used as an inflammatory marker in many diseases.

## Materials and Methods

This retrospective research was performed at the tertiary hospital. We included the patients to the study who had undergone primary tympanoplasty surgery without mastoidectomy because of chronic otitis media. Two groups were designed according to the presence of tympanosclerosis in the middle ear during surgery.

All surgeries were performed under general anesthesia via postauricular incision. To assess presence of tympanosclerosis, microscopic and endoscopic imaging was performed in sinus tympani, supratubal recess, hypotympanium and attic region and tympanosclerosis and the presence of tympanosclerosis were noted in surgical records.

Forty patients who diagnosed tympanosclerosis intraoperatively and 35 subjects whom tympanosclerosis could be not detected in tympanoplasty were enrolled in this retrospective study.

We excluded the subjects in case of presence of chronic adenotonsillar disease or other chronic inflammatory diseases, cardiovascular disorders, allergic rhinitis and renal or liver disease and smoking.

Our retrospective research was planned with respect to the ethical principles of the Declaration of Helsinki.

CBC results were obtained from our medical database. The MPV along with RDW were evaluated using blood samples collected in tubes with dipotassium EDTA by an automated blood cell analyzer within one hour after sampling (Beckman-Coulter LH 780, USA). NLR was accepted as a ratio between the absolute neutrophil and the absolute lymphocyte counts. Moreover, MPV, RDW, neutrophil and lymphocyte counts were compared between the 2 study groups.

**Statistical Analysis:** The participant's numerical variables were evaluated as the mean±standard deviation. The parametric variables of the groups were conducted by an Independent Sample t test. A Chi-squared test was used to evaluate the categorical parameters of the groups. The participant's results were considered to be significant the p result less than 0.05. SPSS® statistics (Version 20.0) was used to perform all analyzes.

## Results

The baseline results of the research population are presented in Table 1. The average age of patients with tympanosclerosis was 23.4±9.2 years, and it was found 24.7±8.9 years in subjects without tympanosclerosis.

There were 21 female and 19 male in subjects with tympanosclerosis and 17 female and 18 male in healthy subjects. Two groups have similar results with respect to age and gender (Table 1).

There was no important difference between two research participants with respect to the MPV, RDW and NLR ( $p > 0.05$ ) (Table 2).

## Discussion

The goal of our present paper was to investigate RDW, MPV and NLR, an easy-to-obtain, noninvasive, inexpensive, and reliable independent indicator of systemic inflammation, in tympanosclerosis patients. For this research, we hypothesized that there was an association between certain markers of systemic inflammation and tympanosclerosis. Nevertheless, no research has been conducted to clarify this issue. In the current paper, our results showed that there is no significant relationship between systemic inflammation markers and tympanosclerosis.

Calcium deposition and hyaline degeneration of middle ear submucosal tissue causes to tympanosclerosis (9). Although there are several hypotheses about etiopathogenesis, it is accepted that tympanosclerosis typically develops secondary to acute and chronic otitis media as well as secondary to ventilation tubes (10).

Although we have not measured oxidative stress markers in the present study, it has been shown that formation of free oxygen radicals is important for the development of tympanosclerosis within the middle ear (3). Researches have emphasized that melatonin, a potent antioxidant, inhibits sclerosis (11). Hence, antioxidant treatment may reduce tympanosclerosis formation. In this context, study of Koc et al. (12) mentioned that the melatonin treatment increased antioxidant levels following myringotomy to reduce development of tympanosclerosis. And also, distortion of balance oxidant-antioxidant and cytokines contribute to the aforementioned initiation and progression of tympanosclerosis (13). On the other hand, association of *H. pylori* and tympanosclerosis were studied to elucidate of etiopathogenesis (14).

The MPV is one of the parameters routinely reported in the complete blood count, and levels of MPV may increase or decrease in chronic inflammation (15). Mean platelet volume gives information about the size of the platelets. The inflammatory and thrombotic cytokines in the platelets increase as MPV increases. It was emphasized that activated or big platelets were depleted in high-grade inflammatory

conditions, or a defective thrombopoiesis resulting from inflammation resulted in decreased MPV (16).

Several studies showed possible link between MPV and systemic and local inflammatory diseases (17). Yazici et al. (18) clarified that MPV levels were significantly higher in rheumatoid arthritis than control groups. They also reported that MPV levels are directly linked with inflammatory markers and prognosis of disease. In a study related to MPV levels in ankylosing spondylitis patients described similar data (17). Moreover, Somuk et al. (19) observed no significant change in MPV values between chronic otitis media with effusion patients and control groups.

Total white blood cell counts and its subtypes are used as common systemic inflammatory indices. Neutrophils are activated by the tissue destruction release enzymes like myeloperoxidase, acid phosphatase, and elastase. The ratio of the leukocytes in the circulation changes during the inflammatory reaction. Neutrophilia is accompanied by relative lymphopenia. The NLR was known as dividing the neutrophil value by the lymphocyte value. The NLR was introduced as a simple marker of the inflammatory reaction (20, 21). In many diseases, such as malignancies, infectious and noninfectious inflammatory pathologies, it has been shown that NLR is useful to predict prognosis and recurrence. Peripheral increased neutrophil count and/or decreased lymphocyte count suggests increased NLR, which is accepted as an important indicator of inflammatory process. Increased NLR has been described as predictive and prognostic factor in some diseases (5, 22, 23).

RDW, a blood marker to assess heterogeneity of RBC obtained in CBC, is used in the differential diagnosis of anemia (24). Increased RDW levels are observed in some situations such as haemolysis, blood transfusion and ineffective erythropoiesis. Elevation in RDW has been shown to be associated primarily with conditions that lead to ineffective production or increased destruction of RBC. Early release of immature, larger RBCs into the circulation results in elevated RDW. Higher RDW appears as chronic inflammation and increased oxidative stress (24). Numerous investigators have clarified that increased RDW levels are linked with prognosis of thromboembolic events, cardiovascular diseases and respiratory diseases (8, 25).

It is known that inflammatory process is center in the etiopathogenesis of tympanosclerosis. However, we could not detect a marked change in the MPV, RDW and NLR levels between participants with and without tympanosclerosis in the present research. Based on a review of the published literature, we did not find any similar results related to the MPV, RDW

and NLR levels in tympanosclerosis. Thus, we are unable to compare our finding with previously published results. Our results will be the first to be published in this area.

We had several limitations of this present study. Firstly, this research was designed retrospectively. Secondly, we did not evaluate the effect of surgery on these blood markers after tympanoplasty. However, our research was planned to clarify whether MPV, RDW and NLR levels may be used as a systemic inflammatory marker of tympanosclerosis.

In summary, we could not find any association between the markers of blood systemic inflammatory and tympanosclerosis. Therefore, tympanosclerosis does not seem to change the systemic inflammation. Originally, it is well known that inflammation may play a crucial role in etiopathogenesis of tympanosclerosis, but more additional larger studies should be done to elucidate this association.

**Conflict of Interest:** The authors do not have any commercial or other association that might pose a conflict of interest. The authors did not have any financial support to write this paper.

**Ethical Approval:** All procedures performed in this study were in accordance with the ethical standards of the institutional committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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