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The Relationship between Tinnitus, Mean Platelet Volume and Neutrophile/ Lymphocyte Ratio-Investigation on the New Focus of the literature

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Abstract:

Introduction: Tinnitus is a condition that occurs through different pathophysiological mechanisms and its underlying reasons are not completely understood. MPV (mean platelet volume) and NLR (neutrophile/lymphocyte ratio) are the parameters that found to be related to many diseases that cause tinnitus.

Objective: The relationship between MPV, NLR and tinnitus are investigated in this study. According to our observations, this is the first study in literature body that investigates these relationships.

Methods: 80 patients with tinnitus and 41 controls were included in the study. Group 1 consisted of males only, group 2 consisted of females only and group 3 consisted of all patient group regardless of their gender. Only the patients with subjective tinnitus aged 18-65, without any active infection and without diagnosed psychiatric disease were included. Age, MPV, NLR, WBC (white blood cell) and platelet counts were used as parameters of investigation.

Results: Comparison of the referred parameters between the patients and controls in each group were resulted as follows: In group 1; age ($p<0.267$), WBC ($p<0.611$), NLR ($p<0.053$), platelet count ($p<0.815$) and MPV ($p<0.033$). In group 2; age ($p<0.579$), WBC ($p<0.209$), platelet count ($p<0.825$), NLR ($p<0.066$) and MPV ($p<0.021$). In group 3; age ($p<0.600$), WBC ($p<0.262$), platelet count ($p<0.363$), MPV ($p<001$) and NLR ($p<0.003$).

Conclusion: The results of this study suggest a statistically significant relationship between tinnitus and MPV and NLR and may help the further studies on this topic.

Keywords: Tinnitus; Mean platelet volume; Wite blood cell count; Platelet count.

Introduction:

Tinnitus can be described as a conscious perception of an inner head sourced sound[1]. Description is regardless of the sound itself, but sounds that persist longer than 5 minutes are defined as tinnitus[2]. It is one of the most common symptoms of the auditory system affecting 17% of general population and 33% of the older population[3]. Tinnitus frequency also increases with aging, equally common for both sexes and 50% of the cases are bilateral[4,5]. Although many metabolic and otological pathologies cause tinnitus, information about its pathophysiology remains a theory only.

MPV (mean platelet volume) is an important parameter for platelet activity. Larger platelets were shown to be enzymatically and metabolically more active[6]. Recent studies have shown that increase in MPV and NLR (neutrophile/lymphocyte ratio)

rates are associated with many diseases such as inflammation, atherosclerosis and cerebrovascular diseases. As we have not encountered any studies relating MPV or NLR to tinnitus, we decided to investigate this point. This study is the first one in the literature body to investigate the relationship between tinnitus and MPV and NLR.

Materials and Methods:

The study protocol was approved by the Clinical Studies Ethics Committee with a protocol number of 10204/31 and each patient signed an informed consent.

This study used CBC (complete blood count) factors of 80 patients with tinnitus that consulted our clinic between the years of 2014 and 2015. 38 patients were male, 42 were female and also 41 healthy people were included in the study as controls. 12 people in the control group were females, 29 were males. Investigated parameters are MPV, NLR, WBC (white blood cell count) and platelet count. Patients with tinnitus who have hearing loss, diagnosed psychiatric disease, active infection, objective tinnitus, aged older than 65 and younger than 18, who smoke regularly were not included the study. All the patients selected for the study had tinnitus for at least 6 months.

Evaluations were made in three different groups of patients. Group 1 included only male patients and male controls, group 2 included only female patients and female controls and group 3 included all the patients and controls regardless of their sex.

All of the investigations were statistically analyzed using SPSS program version 19 (IBM Corporation, NY, US). The comparison between the groups was made with Student's t-test and $P < 0.05$ was considered significant.

Results:

There was no significant difference between the average values of age ($p<0.267$), WBC ($p<0.611$), and platelet count ($p<0.815$) in group 1. Although the statistical significance didn't happen, NLR values were revealed remarkably higher in patient population ($p<0.053$). MPV, on the other hand, was determined higher in patient population with statistical significance ($p<0.033$) (Table 1).

In group 2, no significant difference was observed again in parameters of age ($p<0.579$), WBC ($p<0.209$) and platelet count ($p<0.825$). And also again; NLR values were revealed remarkably higher in patient population ($p<0.066$). MPV parameter was significantly higher in patients with tinnitus than in controls ($p<0.021$) (Table 2).

Age ($p<0.600$), WBC ($p<0.262$) and platelet count ($p<0.363$) parameters did not show any significant difference in group 3 patients compared to controls. However; MPV ($p<0.001$) and NLR ($p<0.003$) parameters were significantly higher than controls (Table 3).

	Patients with tinnitus (n=38) (avg ± SD)	**Control (n=29) (avg ± SD)**	**P value**
Age	48.7 ± 14.4	44.7 ± 10.3	0.267
WBC	7.0 ± 1.5	7.3 ± 1.6	0.611
Platelet Count	250000 ± 59000	247000 ± 45000	0.815
MPV	9.26 ± 1.14	8.54 ± 1.07	**0.033***
nlr	2.47 ± 0.48	2.11 ± 0.69	0.053

Table 1: Comparison of male patients' and controls' (Group 1) average values.

	Patients with tinnitus (n=42) (avg ± SD)	**Control (n=12) (avg ± SD)**	**P value**
Age	45.7 ± 10.9	48.2 ± 14.3	0.579
WBC	7.0 ± 1.3	7.5 ± 1.5	0.209
Platelet Count	284000 ± 60000	274000 ± 73000	0.825
MPV	9.60 ± 1.06	8.60 ± 1.24	**0.021***
nlr	2.69 ± 0.33	2.12 ± 1.30	0.066

(WBC: White blood cell count, MPV: Mean platelet volume, nlr: Neutrophile to lyphocite ratio, *: statistically significant)

Table 2: Comparison of female patients' and controls' (Group 2) average values.

	Patients with tinnitus (n=80) (avg ± SD)	Control (n=41) (avg ± SD)	P value
Age	47.1 ± 12.6	45.7 ± 11.5	0.600
WBC	7.0 ± 1.4	7.4 ± 1.6	0.262
Platelet	268000 ± 61000	256000 ± 56000	0.363
MPV	9.44 ± 1.10	8.5 ± 1.11	**0.001***
nlr	2.59 ± 0.42	2.11 ± 0.89	**0.003***

(WBC: White blood cell count, MPV: Mean platelet volume, nlr: Neutrophile to lyphocite ratio, *: statistically significant)

Table 3: Comparison of all patients' and controls' (Group 3) average values.

Discussion:

In this study, we aimed to investigate the relationship of tinnitus with MPV and NLR while trying to put forth the factors in tinnitus aetiopathogenesis.

Moller et al. stated that the tinnitus sound was perceived as many nerve fibers have increased activity spontaneously[7]. Feldman's position theory suggested that when the defective cuticular membrane forms as a result of the depolarization of ciliated cells, a special part of the organ of corti is activated and tinnitus is formed[8].

Tinnitus is usually observed together with cochlear damage. It is believed that tinnitus is caused because of the spontaneous increase in firing rates of auditory nerve fibers as a result of hyperactivity in ciliated cells. This hypothesis showed that tinnitus can be formed without increase in spontaneous activity as spontaneous activity actually decreases in tinnitus resulting from noise and aminoglycoside exposure[7]. Jastreboff and Hazel showed that most patients with tinnitus had damage in the cochlea or the 8th nerve and suggested that the reason for tinnitus could be peripheral systems[9]. Tunndorf, on the other hand, suggested tinnitus can arise from all auditory pathways[10]. According to him, the primary reason for tinnitus is the chemical imbalance between cell membrane and stereocilia. He suggests, as a result of this imbalance even very small spontaneous activity would be perceived by vibrant cells and nerve fibers causing tinnitus[10]. Metabolic conditions as well as otological ones can cause tinnitus. For example, it is shown that patients with cardiac insufficiency, atherosclerosis, hypertension and anemia are prone to form tinnitus related to low endocochlear potentials[11,12]. Tinnitus was also detected together with hypothyroidism and hyperthyroidism[13]. In diabetic patients, tinnitus was observed as a result of citria vascularis and thickening of the basal membrane[12,13].

MPV is an important indicator of platelet activity. Larger platelets are shown to be enzymatically and metabolically more active[6]. Large platelets are more adhesive and tend to aggregate more than smaller ones[14]. This increase in platelet volume increases the tendency for coronary thrombus formation in acute coronary syndrome patients[15]. MPV is also used as a marker for atherosclerosis[16]. Many clinical studies detected MPV to be associated to atherosclerosis and cardiac diseases[17,18]. MPV scores were significantly higher in acute ischemic shock than in control group[19-21]. In patients with diabetes, MPV was higher compared to the normal glycemic controls; in addition, it has been proposed that an increase in MPV could play a role in the micro- and macro-vascular complications related to diabetes[22]. Several studies show that MPV increases significantly in hyperthyroidism[23] and hypothyroidism[24]. When we investigate the relationship of tinnitus with MPV which is increased in many metabolic conditions that cause tinnitus, we observed that MPV was significantly higher in all three groups (group 1 $p<0.033$, group 2 $p<0.021$, group 3 $p<0.001$) compared to the controls. This situation is in accordance with the literature body.

NLR parameter is also increased in many diseases that cause tinnitus. Many studies show that neutrophile and lymphocyte numbers are important for peripheral inflammation and atherosclerotic process[25,26]. Increase in NLR is found to act in atherosclerotic process and cardiovascular disease[27-29]. A study on patients with stroke reported that CRP (C-reactive protein) which is an inflammation marker is significantly correlated with increase in NLR ($p<0.001$)[28]. Verdoia et al. reported that NLR was significantly increased in patients with diabetes and there is a significant correlation between increased NLR and coronary artery disease[30].

In our study, although NLR was found to be prominently higher in patients with tinnitus in group 1 and group 2, the difference could not reach a statistically significant level ($p<0.053$ and $p<0.066$

respectively). Difference of NLR in patients with tinnitus and controls was statistically significant in group 3 ($p<0.003$).

This study reports that NLR and MPV are increased in patients with tinnitus, as well as in the pathologies that cause tinnitus. Other parameters investigated in relation to tinnitus in this study such as age, WBC and platelet count were not significantly different than the controls.

Tinnitus is a condition that can be caused by many different mechanisms and pathologies. Here, we wanted to state the significant increase in NLR and MPV in many different pathological conditions that cause tinnitus through our literature examination. The statistical analysis of our data suggests a significant correlation between tinnitus and the increase in MPV and NLR for the first time. Consequently, this study is the first one to investigate the relationship of tinnitus with NLR and MPV through literature search and analyses and further studies are required to clarify the information on this topic.

Conclusion:

The results of this study suggest a statistically significant relationship between tinnitus and MPV and NLR and may help the further studies on this topic. Our results may canalize the further studies about tinnitus pathophysiology to blood circulation and vascular mechanisms. Also the other inflammation and vascular pathology markers would be a needed topic to study on tinnitus.

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Ethical Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/ or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflict of Interest: None of the authors has any conflict of interest, financial or otherwise.

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