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Research

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The Relationship Between Tonsillar Size and Neutrophil-to-Lymphocyte Ratio in Children With Recurrent Tonsillitis

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ABSTRACT

Objectives: To explore the relationships between tonsillar sizes and neutrophil-to-lymphocyte ratio (NLR) values in children with recurrent tonsillitis.
Subjects and Methods: In total, 236 children (128 males, 108 females; average age 11.80±9.16 years; range, 4-18 years) who underwent tonsillectomy with a diagnosis of recurrent tonsillitis were included. The patients were divided into four groups according to the tonsillar sizes. Group A was consist of 56 children with grade 1 tonsil size, while group B, C and D was consist of 58, 70 and 52 children with grade 2, 3 and 4 tonsil size, respectively. Pre-operative NLR values of all groups were compared with measurements in the post-operative third month.
Results: In group A, pre-operative NLR levels were 1.76±0.92, while post-operative NLR were 1.74±1.53. No statistically significant difference in NLR values was observed between pre- and post-operatively in group A (p=0.864). In group B, pre-operative NLR levels were 1.56±1.14, while post-operative NLR were 1.29±0.65. In group C, pre-operative NLR levels were 1.48±1.47, while post-operative NLR were 1.22±0.79. In group D, pre-operative NLR levels were 1.44±1.52, while post-operative NLR were 1.19±0.96. Post-operative NLR values were significantly lower than pre-operative NLR values in both groups B, C, D (p=0.012, p=0.036, p=0.043, respectively).
Conclusion: The larger tonsils affect the NLR levels and larger tonsils are strongly suspected to contribute to higher systemic inflammations. However, higher systemic inflammations can be prevented by tonsillectomy.

KEYWORDS: Tonsillar sizes; Neutrophil-to-lymphocyte; Recurrent tonsillitis.

ABBREVIATIONS: NLR: Neutrophil-to-lymphocyte ratio; OSAS: Obstructive Sleep Apnea Syndrome; IEC: Institutional Ethics Committee; EDTA: Ethylene-diamine-tetracetic acid.

INTRODUCTION

Acute tonsillitis is usually diagnosed by clinical acute inflammatory manifestations such as hyperemic tonsils, exudation, and ulceration.[1,2] Approximately 5 to 17% of cases are bacteriological which is mostly group A beta-hemolytic streptococci, although the most common etiological agent is viral.[3] As previously described by Paradise, recurrent tonsillitis is defined as seven episodes within one year or five episodes in the preceding two years and more or three episodes in the preceding three years and more.[4] Many factors are blamed for the development of recurrent tonsillitis. These include patient incompliance, premature cessation of antibiotherapy, inadequate antibiotic absorbance, bacterial tolerance, bacterial load, bacterial biofilms, and immune system deficiencies.[2,3]

The most common indications of tonsillectomy or adenotonsillectomy are obstructive sleep apnea syndrome (OSAS) due to adenotonsillar hypertrophy, followed by recurrent

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tonsillitis.[5-10] Large tonsils obstruct the upper airway and it is associated with symptoms of upper airway obstruction including mouth breathing, snoring, sleep apnea, coughing at night, and production of hyponasal sounds as well as sinusitis and recurrent otitis media.[8-11] Poor quality sleep and sleep-related hypoxia have been previously described in children with recurrent tonsillitis. Capper and Canter[9] reported that children awaiting tonsillectomy have poorer sleep quality than their normal peers. However, there is no dose-response effect between deteriorating sleep quality and increasing frequency of tonsillitis.[9] Recurrent infections lead to some changes in hematological parameters. Recently, neutrophil-to-lymphocyte ratio (NLR) was explored in some diseases such as vestibular neuronitis, Bell's palsy, sudden hearing loss, OSAS in the field of otorhinolaryngology.[12-18] Neutrophils are essential for cytokine production in acute process in inflammatory disorders while lymphocyte is important for cytokine production in chronic process in inflammatory disorders.[19] Also, higher neutrophils demonstrate an acute inflammation and lower lymphocytes demonstrate deficiency of some elements in body and chronic inflammatory status. NLR is propounded as a parameter of systemic inflammation.[5-7] NLR can be easily determined by a simple complete blood count analysis and is a valuable parameter in diseases such as sudden hearing loss, certain some cancers, autoimmune and cardiovascular diseases.[6-14] Only a few studies have explored the relationship between NLR levels and recurrent tonsillitis. To the best of our knowledge, no study has yet focused on associations between tonsillar sizes and NLR values. We address this topic in the present study. In the present study, the relationships between tonsillar sizes and NLR values in children with recurrent tonsillitis were explored.

MATERIALS AND METHODS

We retrospectively reviewed data collected from January 2009 to September 2012 on patients treated in the Department of Otolaryngology, Head-and-Neck Surgery, of our hospital. In total, 236 children who underwent tonsillectomy with a diagnosis of recurrent tonsillitis were included in the study. Patients with previous history of adenotonsillectomy, genetic syndromes, congenital malformations, cleft palate, nasal septal deviation, sinonasal infection, chronic diseases, hematological diseases were excluded from the study. All parents of the patients were informed about the study and a written consent was obtained from each parents of the patients. The study protocol was approved by the Institutional Ethics Committee (IEC). The study was conducted in accordance with the principles of Helsinki declaration. All patients were followed for at least 1 year and the total number of acute tonsillitis episodes was recorded. Recurrent tonsillitis that previously described by Paradise,[4] is defined as seven episodes within 1 year or 5 episodes in the preceding 2 years and more or 3 episodes in the preceding 3 years and more. Recurrent tonsillitis was considered as an indication for tonsillectomy and these patients were recommended for tonsillectomy. All tonsillar sizes were evaluated by the same otorhinolaryngologist using Brodsky[20] grading scale as follows:

- +1: Tonsils obstruct less than 25% of the upper airway.
- +2: Tonsils obstruct 25-50% of the upper airway.
- +3:Tonsils obstruct 50-75% of the upper airway.
- +4: Tonsils obstruct more than 75% of the upper airway.

The patients included in the study were divided into 4 groups according to the tonsillar sizes. Group A was consist of 56 children with grade 1 tonsil size, while group B, C and D was consist of 58, 70 and 52 children with grade 2, 3 and 4 tonsil size, respectively. All operations risks and complications were explained to children's parents. Tonsillectomy was performed *via* cold-steel dissection approach. All the operations were performed by the same otorhinolaryngologist in our department. All chidren were clinically no symptoms of infection at the time of tonsillectomy. Routine pre-operative blood samples were taken from the antecubital vein into tubes with ethylene-diamine-tetracetic acid (EDTA) by a nurse. Neutrophil and lymphocyte were measured by hematology analyzer machine. NLR was calculated from the differential count by dividing the neutrophil measurement by the lymphocyte measurement. All of the patients were invited for control examinations at post-operative first week and third month. Blood samples were taken again in the post-operative third month, and the measurements were compared with pre-operative measurements.

Statistical Analysis

Number Cruncher Statistical System (NCSS) 2007 software (Kaysville, UT, USA) was used for all statistical analyses. Descriptive statistics (means and standard deviation, medians with interquartile range) were derived. The significance of intergroup differences was analyzed using Student's *t*-test, and the significance of the medians was analyzed with the Mann-Whitney U-test. A paired *t*-test was performed to test differences between pre-operative and post-operative values of NLR. A p-value<0.05 was considered to reflect statistical significance.

RESULTS

We included 236 patients: 108 (45.8%) females and 128 (54.2%) males. Their average age was 11.80±9.16 years (range: 4-18 years). The age and gender were not significantly different between the groups (all p>0.05). In group A, mean pre-operative NLR levels were 1.76±0.92, while post-operative NLR values were 1.74±1.53. No statistically significant difference in mean NLR values was observed between pre- and post-operatively in group A (p=0.864, Figure 1). In group B, mean pre-operative NLR levels were 1.56±1.14, while post-operative NLR values were 1.29±0.65. Post-operative NLR values were significantly lower than pre-operative NLR values in group B ($p=0.012$, p<0.05). In group C, mean pre-operative NLR levels were 1.48±1.47, while post-operative NLR values were 1.22±0.79. Post-operative NLR values were significantly lower than pre-operative NLR values in group C (p=0.036, p<0.05). In group D, mean pre-operative NLR levels were 1.44±1.52, while post-

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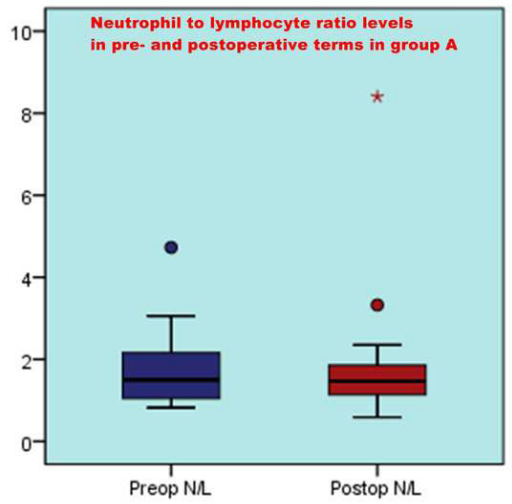

Figure 1: Neutrophil to lymphocyte ratio levels in pre- and post-operative terms in group A.

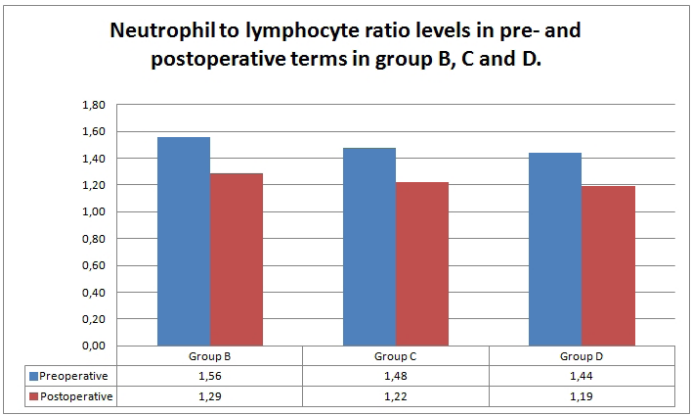

Figure 2: Neutrophil to lymphocyte ratio levels in pre- and post-operative terms in group B, C and D.

NLR	Group A (n:56)	Group B (n:58)	Group C (n:70)	Group D (n:52)
pre-operative	1.76±0.92	1.56±1.14	1.48±1.47	1.44±1.52
post-operative	1.74±1.53	1.29±0.65	1.22±0.79	1.19±0.96
*p	0.864	0.012	0.036	0.043

NLR: Neutrophil-to-lymphocyte ratio; *p: Mann–Whitney U-test; *p<0.05

Table 1: Comparison of Neutrophil-to-Lymphocyte ratio between groups.

operative NLR values were 1.19±0.96. Post-operative NLR values were significantly lower than pre-operative NLR values in group D (p=0.043, p<0.05) (Table 1) (Figure 2).

DISCUSSION

Identification of etiological factors of recurrent tonsillitis remains a current issue in otorhinolaryngology. Although many factors are blamed for the development of recurrent tonsillitis, there is no consensus on the certain etiological factors of recurrent tonsillitis. Knowledge of such factors would reduce the cost of surgery, increase the quality of life, and allow child development to be optimized.[1,2] Indications of tonsillectomy are well defined previously in literature, however, it depends entirely on surgeons approach and definitions. Also, child age, number of acute tonsillitis episodes, environmental conditions, the level of country development, parents attention affect the decision of timing of surgery.[2,4] No consensus has yet emerged regarding the optimal age at surgery, the surgical procedure to be used, or optimal post-operative care. Lack of data hinders the resolution of several controversial issues. Recently, NLR was used for determining the disease-specific survival of cancer subjects.[21] Also, systemic inflammation is strongly suspected to contribute to the decreased the overall survival of cancer subjects.[21-23] Similarly, the study of Gibson et al[23] have reported that survival rates after coronary artery bypass grafting were decreased due to higher NLR values. Some authors subscribe to that NLR is a valuable predictive marker for disease-specific survival and the overall of cancer subjects.[21,22] However, the exact reason of systemic inflammation in cancer subjects remains unclear. The study of Köseoğlu et al[5] have reported that mean NLR values of the OSAS group was 1.88±0.85 and NLR values of control group was 2.01±0.85 and they found no significant differences between OSAS group and normal group in terms of NLR values. Also, they assert that NLR may be used as a marker that indicates chronic intermittent hypoxia in patients with OSAS.[5] In another study, Chung et al[14] reported that NLR was higher in patients with vestibular neuronitis. NLR levels increased with nystagmus lasting up more than five days and drug treatment required for such patients. The study of Baglam et al[13] have reported that NLR was higher in patients who developed deep neck infection while compared to those who did not develop among children with acute bacterial tonsillitis. The study of Yenigun[24] have reported that the NLR could be used in chronic tonsillitis subjects as a potential helpful method for defined the necessity and timing of tonsillectomy and post-operative follow-up. To our knowledge, the present study provides the first report of explored the relationships between NLR and tonsillar sizes in children with recurrent tonsillitis. In the present study, the patients included were divided into four groups according to the tonsillar sizes. No statistically significant difference in mean NLR values was observed between pre- and post-operatively in group A, in contrast to other groups. We could assert that tonsillar sizes affect the NLR values and larger tonsils are strongly suspected to contribute to higher systemic inflammations. Also, surgeon do not decide tonsillectomy due to tonsillar size, but our data suggest that tonsillar sizes affect the systemic inflammation and may be contribute to increase numbers of acute tonsillitis episode. However, tonsils have an endophytic growth pattern. Moreover, it is not yet known the reason why some patients develop tonsil-

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lar hypertrophy and some do not. Recurrent tonsillitis decrease the quality of children's life, therefore, timing of surgery is very important.[2,3] Also, without timely and appropriate treatment of recurrent tonsillitis, complications could be occurred.[4] Its complications are serious and life-threatening including such as peritonsillar, parapharyngeal and retropharyngeal abscesses.[11] Also, Yenigun[24] suggested that NLR levels could be used to prevent complications due to delayed or inadequate treatment in children with chronic tonsillitis. Therefore, several studies in the literature have led to the emergence of a new controversy. On the other hand, there are some limitations to this study. The limitations of this study included a retrospective study design, the sample size, and the lack of randomization. Again, NLR levels were not correlated with recurrent tonsillitis severity evaluations such as number of acute tonsillitis episode, symptom scores or the quality of life. However, a determination of severity of recurrent tonsillitis is objectively difficult because the diagnostic criteria is not determined. Future randomized studies should assess the relationship between number of acute tonsillitis episodes and NLR values in larger numbers of patients.

CONCLUSION

In conclusion, the larger tonsils affect the NLR levels and larger tonsils are strongly suspected to contribute to higher systemic inflammations. However, higher systemic inflammations can be prevented by tonsillectomy. Future randomized studies should assess the relationship between number of acute tonsillitis episodes and NLR values in larger numbers of patients.

AUTHORS CONTRIBUTIONS

YY and MÇ conceived, designed and did statistical analysis & editing of manuscript. BO, BMŞ, FTK did data collection and manuscript writing. FTK performed operations and did review and final approval of manuscript.

CONFLICTS OF INTEREST

No conflicts of interest was declared by the authors.

FINANCIAL DISCLOSURE

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