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The Role of Tonsils in the Development of Covid-19 Pneumonia

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ABSTRACT

Objective: Despite extensive research, the physiopathology and clinical course of novel coronavirus disease 2019 (COVID-19) is still not fully understood. It is not known why some COVID-19 patients develop pneumonia while others are asymptomatic or have only mild upper respiratory tract symptoms. The tonsils are an element of the immune system that provide first-line defense against microorganisms entering the body via the upper respiratory tract. This study aimed to evaluate the role of tonsils in preventing the development of COVID-19 pneumonia. **Materials and Methods:** The study included 198 patients aged 20-40 years who presented to the pandemic outpatient clinic, had confirmed COVID-19 infection, and had no comorbidities. The relationship between lung involvement and history of tonsillectomy was analyzed. **Results:** Of the 198 patients in the study, 108 were male, 90 were female, and the mean age was 34.7 years. Eighty-three (41.9%) of the patients did not have lung involvement and 115 (58.1%) had lung involvement. Twelve (10.4%) of the patients with lung involvement and 3 (3.6%) of the patients without lung involvement had a history of tonsillectomy. The prevalence of pneumonia did not differ statistically between the groups ($p>0.05$). **Conclusion:** Although there was no statistically significant relationship between COVID-19 pneumonia and tonsillectomy in this study, we observed that pneumonia developed in 80% of the 15 patients who underwent tonsillectomy. This suggests that greater caution in terms of lung involvement may be warranted for tonsillectomized patients with COVID-19.

Keywords: Tonsillectomy, COVID-19, Pneumonia, Immunity.

Covid-19 Pnömonisinin Gelişiminde Tonsillerin Rolü

ÖZ

Amaç: COVID-19 hastalığı fizyopatolojisi ve klinik seyri yapılan pek çok bilimsel araştırmaya rağmen henüz tam olarak çözülememiştir. Yeni tip koronavirüs pandemisinde neden bazı hastalarda pnömoni gelişirken, bazı hastalarda sadece üst solunum yolu bulguları ile hatta bazen asemptomatik seyrettiği bilinmemektedir. Bu klinik farklılığın sebeplerinin ortaya konabilmesi için çalışmalara ihtiyaç vardır. Bu çalışmada üst solunum yolu ile vücuda giren mikroorganizmalara karşı ilk savunmayı sağlayan, immün sistemin bir elemanı olan tonsillerin COVID-19 pnömonisi gelişimini önlemedeki rolünün araştırılması amaçlanmıştır. **Gereç ve Yöntem:** Pandemi polikliniğine başvuran, yeni tip koronavirüs ile enfekte, 20-40 yaş arası, ek hastalığı olmayan 198 hasta çalışmaya dahil edildi. Hastaların akciğer tutulumlarının olup olmadığı, tonsillektomi olup olmadığı incelenerek akciğer tutulumu ile tonsillektomi öyküsü arasındaki ilişki değerlendirildi. **Bulgular:** Çalışmaya dahil edilen 198 hastanın 108'i erkek, 90'ı kadın ve yaş ortalaması 34.73 idi. Hastaların 83'ünde akciğer tutulumu bulunmazken, 115'inde akciğer tutulumu olan hastaların 12'sinde tonsillektomi öyküsü mevcut iken, akciğer tutulumu olmayan hastaların 3'ünde tonsillektomi öyküsü mevcuttu. **Sonuç:** Pnömoni gelişmesi ve tonsillektomi arasında istatistiksel olarak anlamlı sonuç bulunamadı ($p>0.05$), ancak tonsillektomi olan 15 hastanın %80'inde pnömoni gelişirken %20'sinde gelişmediği görüldü. Bu nedenle tonsillektomi öyküsü olan hastalarda COVID-19 enfeksiyonu gelişmesi durumunda akciğer tutulumu açısından daha dikkatli olunmalıdır.

Anahtar Kelimeler: Tonsillektomi, COVID-19, Pnömoni, İmmünite.

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INTRODUCTION

Coronaviruses have an unsegmented, single-stranded, positive-sense RNA genome of approximately 30 kb, giving them the largest known RNA virus genomes. Coronaviruses are common among mammals and birds and cause a range of diseases that affect many organ systems.

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The first case was encountered in December 2019 in Wuhan city of the Hubei province of China. Since then, COVID-19 has continued to spread, causing a pandemic that continues to the present day. The first case in our country was reported on March 11, 2020. The clinical presentation of COVID-19 infection ranges from asymptomatic to severe; symptoms usually include fever, myalgia, malaise, cough, and (in moderate to severe cases) shortness of breath. Despite many scientific studies, the physiopathology and clinical course of COVID-19 remains incompletely understood. It is still not known why some patients with COVID-19 develop pneumonia, while others have asymptomatic infection or develop only mild upper respiratory tract symptoms.

The tonsils are members of the Waldeyer ring, which forms the first line of defense against bacteria and viruses that enter the body by inhalation or ingestion (Suzumoto, 2006; Nave et al., 2001). Although the rate varies by country, tonsillectomy is one of the most frequently performed surgical interventions worldwide. The effects of tonsillectomy on immunity are still controversial. While some publications argue that both humoral and cellular immunity are adversely affected after tonsillectomy (Ogra, 1976; Cantani et al., 1986), some argue that it has no negative effects (Zielnik-Jurkiewicz et al., 2002; Kaygusuz et al., 2009). In this study we aimed to investigate the role of tonsils in the development of COVID-19 pneumonia.

MATERIALS AND METHODS

Procedures

The study included 198 patients who presented to the pandemic outpatient clinic and had confirmed COVID-19 infection (positive polymerase chain reaction test for SARS-CoV-2). All of those included in the study were patients between the ages of 20 and 40 without any comorbid diseases. Patients outside the specified age ranges, with any additional disease, and in need of intensive care due to cytokine storm were not included in the study. We determined the patients' age, gender, presence of pulmonary involvement, and tonsillectomy history and evaluated the relationship between lung involvement and history of tonsillectomy (table 1).

Statistical analysis

Statistical analyses were performed using SPSS version 23.0 software. Conformity of the variables to normal distribution was examined using visual

(histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Descriptive analyses were given using mean and standard deviation for normally distributed variables. Categorical data were evaluated with the chi-square test. A p-value less than 0.05 was considered statistically significant (table 2).

Ethical considerations

Ethics committee approval for the study was obtained from Ethics Committee (dated 21/01/2021, number 273).

RESULTS

Of the 198 patients included in the study, 108 were men, 90 were women, and the mean age was 34.7 years. Pulmonary involvement was detected in 115 of the patients, while 83 patients did not have lung involvement. A total of 15 patients had a history of tonsillectomy, 12 of whom had lung involvement and 3 of whom did not have lung involvement. The prevalence of pneumonia was 56.3% among patients with no history of tonsillectomy, compared to 80% among patients with a history of tonsillectomy. Although pneumonia tended to occur more often in patients with a history of tonsillectomy, the relationship did not show statistical significance in the chi-square test ($p > 0.05$).

Table 1. Basic demographic and clinical characteristics of the patients.

| | | n | % |
|----------------------|--------|------------|-------|
| Gender | Male | 108 | 54.55 |
| | Female | 90 | 45.45 |
| Pneumonia | No | 83 | 41.92 |
| | Yes | 115 | 58.08 |
| Tonsillectomy | No | 183 | 92.42 |
| | Yes | 15 | 7.58 |
| Age Mean±SD | | 34.73±7.20 | 36.00 |

SD=Standard deviation.

Table 2. Comparison of COVID-19 pneumonia prevalence according to tonsillectomy history.

| | | Tonsillectomy | | | | *p |
|------------------|-----|---------------|-------|-----|-------|-------|
| | | No | | Yes | | |
| | | n | % | n | % | |
| Pneumonia | No | 80 | 43.72 | 3 | 20.00 | 0.074 |
| | Yes | 103 | 56.28 | 12 | 80.00 | |

*Chi-Square test.

DISCUSSION

Tonsillectomy is one of the most common surgical interventions worldwide, although its frequency varies from country to country and even in different regions of the same country. In the United States, one-third of all surgical interventions performed in the 1930s were tonsillectomies, and in England 50-75% of children had their tonsils removed (Rosenfeld, 1990).

In Finland, the frequency of adenoidectomy in childhood has been reported as 24%, and the frequency of tonsillectomy has been reported as 8% (Mattila, 2001). A study conducted in Turkey demonstrated relatively low rates of tonsillectomy (4.9%), adenoidectomy (2.7%), and adenotonsillectomy (2.1%) compared to the literature. In our study, 15 of 198 patients (7.6%) had a history of tonsillectomy. The palatine tonsils are located in the oropharynx, which is the common entry site of the gastrointestinal and respiratory tracts. Thanks to this important position, they are one of the lymphoid organs that provide the first immune response against antigens that enter the body through the mouth and nose. Waldeyer first described the Waldeyer ring formed by the nasopharyngeal adenoid tissue, palatine tonsils, and lingual tonsils in 1884, and the main component of this ring is the palatine tonsils (Nave et al., 2001). There are various studies in the literature on the effects of tonsillectomy on the immune system, but these studies have yielded conflicting results. Böch et al. followed tonsillectomized patients for a mean of 6.6 ± 2.1 years and reported that while the overall infection frequency did not increase, immunoglobulin A levels in tonsillectomized patients were significantly lower while immunoglobulin M and G levels did not change (Böch et al., 1994). Byars et al. evaluated the follow-up of children who underwent tonsillectomy at age 0-9 years until the age of 30 years and found that there was an approximately three-fold increase in upper respiratory tract infections and a 17% increase in infectious diseases (Byars et al., 2018). Kaygusuz et al. evaluated humoral and cellular immune parameters in 54 patients with tonsillectomy at postoperative 1 month and 54 months and reported that these parameters were normal in the long term after tonsillectomy, with no differences from a control group in the same age range (Kaygusuz et al., 2009). Yan et al. evaluated serum complement and immunoglobulin levels at postoperative 1 and 3 months to evaluate the effect of tonsillectomy on immunity in children under the age of 3 years. They reported that immunoglobulin A levels decreased in the early period but improved later, with no increase in the frequency of infection (Yan, 2019). Johansson and Hultcrantz compared 18 tonsillectomized patients at a mean of 20 years after tonsillectomy with age-matched non-tonsillectomized patients and observed no difference between the two groups in lower respiratory tract or other infectious diseases. They noted that the prevalence of chronic diseases was higher in patients with tonsillectomy, but they did not evaluate this as significant due to the small sample size (Johansson & Hultcrantz, 2003). In another cohort study, no increase was found in the frequency of acute upper respiratory tract infections in patients with tonsillectomy, but an increase in the frequency of asthma was reported (Song et al., 2021).

In our study, there was no significant difference in tonsillectomy rate between patients who developed COVID-19 pneumonia and those who did not, but the rate of pneumonia was higher in tonsillectomized patients. As in Johansson and Hultcrantz's study, the number of tonsillectomized patients in our study was small. Larger study groups may provide more meaningful results. The symptoms of COVID-19 range from asymptomatic disease to acute respiratory distress syndrome and multiorgan failure, which can end in death. It remains a mystery why the disease has such a wide spectrum of symptoms. The lungs are the most damaged organs, and the presence of pulmonary involvement is one of the main parameters used to define COVID-19 clinical severity. Various rates of lung involvement have been reported in the literature, including 43.7% in a study by Ozdemir et al. and 86.2% in a study by Guan et al. In our study, the prevalence of lung involvement was 58.1% overall, 56.6% in non-tonsillectomized patients, and 80% in tonsillectomized patients. Although the difference was not statistically significant, the rate of pneumonia development was higher in the tonsillectomy group. Studies on the localization of the sars cov-2 virus in the tonsils have also shown the presence of the virus in the tonsils of COVID-19 patients. Xu et al, in their study, using samples from 110 children undergoing tonsillectomy and adenoidectomy during the COVID-19 pandemic, they identified 24 samples with evidence of previous SARS-CoV-2 infection, and their results provide evidence for persistent tissue-specific immunity to SARS-CoV-2 in the upper respiratory tract of children after infection (Xu et al., 2022). Tan et al; concluded the tonsils are a secondary lymphoid organ that develop germinal center responses to SARS-CoV-2 infection and could play a role in the long-term development of immunity (Tan et al., 2022). These studies also report that the tonsils are among the organs that are effective in COVID-19 immunity, and they support the explanation of the high rate of pneumonia in patients with tonsillectomy in our study. In our literature search, we found two other studies on the clinical course of COVID-19 disease in tonsillectomized patients. In a study by Doblán and Doblán, no statistically significant difference was found between COVID-19 patients with and without a history of tonsillectomy in terms of age, gender, body mass index, comorbid diseases, or length of hospital stay, whereas the prevalence of symptomatic infection was significantly higher among tonsillectomized patients compared to non-tonsillectomized patients (Doblán, 2021). In addition, a multicenter study by Capriotti et al. evaluated whether there was a difference in symptoms in 779 COVID-19 patients with and without a history of tonsillectomy. While fever, chills, and fatigue were significantly more frequent in tonsillectomized patients, no difference was found

between the two groups in terms of length of hospital stay (Capriotti, 2021). Neither study provided information regarding the development of pneumonia, and to the best of our knowledge, our study is the first in the literature to evaluate this difference.

CONCLUSION

Although there was no statistically significant difference in the development of pneumonia based on tonsillectomy history, we observed that pneumonia developed in 80% of patients who underwent tonsillectomy compared to 56.3% of patients with no history of tonsillectomy. Therefore, greater caution in terms of lung involvement may be warranted for tonsillectomized patients with Covid-19.

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Conflict of Interest

The author declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Author Contributions

Plan, design: SBC, İÖ; **Material, methods and data collection:** MA, AK; **Data analysis and comments:** YK; **Writing and corrections:** SBC, İÖ.

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