doi: 10.53446/actamednicomedia.1475004

Acta Medica Nicomedia

Cilt: 8 Sayı: 1 Şubat 2025 / Vol: 8 Issue: 1 February 2025
https://dergipark.org.tr/tr/pub/actamednicomedia

Research Article | Araştırma Makalesi

THE EFFECT OF PREVIOUS ADENOTONSILLECTOMY ON THE RISK OF CONTRACTING COVID-19 AND THE SEVERITY OF THE DISEASE IN PEDIATRIC POPULATION

PEDİATRİK POPÜLASYONDA GEÇİRİLMİŞ ADENOTONSİLLEKTOMİNİN COVID-19'A YAKALANMA RİSKİ VE HASTALIĞIN ŞİDDETİ ÜZERİNDEKİ ETKİSİ

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ABSTRACT

Objective: The effect of the Waldeyer's lymphatic ring at the entry point of respiratory pathogens has essential functions in forming the immune response in childhood, and its effect on the frequency and severity of Coronavirus disease 2019 (Covid-19) is not clearly known. The objective of this study is to analyze the occurrence and severity of Covid-19 in pediatric patients undergoing adenotonsillectomy surgery.

Methods: Patients aged 3-15 with a history of adenotonsillectomy were compared to a control group in terms of the incidence and severity of Covid-19.

Results: In patients undergoing adenotonsillectomy, a Covid test positivity rate of 1.5% was observed, compared to 2.7% in the control group, indicating a statistically significant difference. However, there was no disparity between the two groups regarding disease severity.

Conclusion: Adenotonsillectomy does not elevate the risk of Covid 19 infection in children. In fact, individuals who have undergone this surgery exhibit a decreased incidence of Covid-19 infection.

Keywords: COVID-19, coronavirus, adenotonsillectomy, immunity

ÖZ

Amaç: Solunum yolu patojenlerinin giriş noktasındaki Waldeyer lenfatik halkasının etkisi, çocukluk çağında immün yanıtın oluşmasında önemli işlevlere sahip olup, Covid-19 hastalığının sıklığı ve şiddeti üzerine etkisi net olarak bilinmemektedir. Bu çalışmanın amacı adenotonsillektomi ameliyatı geçiren çocuk hastalarda Covid-19 hastalığının ortaya çıkışını ve ciddiyetini analiz etmektir.

Yöntem: Adenotonsillektomi öyküsü olan 3-15 yaş arası hastalar, Covid-19 hastalığının görülme sıklığı ve şiddeti açısından kontrol grubuyla karşılaştırıldı.

Bulgular: Adenotonsillektomi yapılan hastalarda Covid testi pozitiflik oranı %1,5, kontrol grubunda ise %2,7 olarak görüldü ve bu da istatistiksel olarak anlamlı bir farka işaret ediyor. Ancak hastalığın şiddeti açısından iki grup arasında fark yoktu.

Sonuç: Adenotonsillektomi çocuklarda Covid 19 enfeksiyonu riskini artırmamaktadır. Aslında bu ameliyatı geçiren kişilerde Covid-19 enfeksiyonu görülme sıklığında azalma görülüyor.

Anahtar Kelimeler: COVİD-19, coronavirüs, adenotonsillektomi, bağışıklık

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Submitted/Başvuru: 07.05.2024 • **Accepted/Kabul:** 16.12.2024 • **Published Online/Online Yayın:** 28.02.2025

Introduction

Coronavirus disease 2019 (Covid-19), caused by the 2019 novel coronavirus (SARS–CoV–2), may cause severe systemic organ failures. According to data from the World Health Organization (WHO), since the beginning of the pandemic, around 250 million cases of Covid-19 have been diagnosed, resulting in approximately 5 million deaths.[1] It is known that children under the age of 5 account for approximately 1.8% of the total cases, and children between the ages of 5-15 make up 6.3% of the total cases. It has been determined that the rate of the population aged 15 and under in total deaths is 0.2%.[1] According to the American Academy of Pediatrics' data, the mortality rate in individuals who had Covid-19 in childhood in the United States is 0.03%.[2]

Although some of the factors, such as; age, gender, chronic diseases, smoking exposure, and immune system response, are emphasized for the severity differences of the disease, the exact reasons are unknown. However, it is a fact that it is milder in the pediatric group.[3,4] Various hypotheses have been proposed to explain the reasons for this difference. For example, in the pediatric age group, other viruses may compete with SARS-CoV-2 in the mucosa of the lung and respiratory tract and limit spreading of the virus or low expressions of the angiotensin - converting enzyme-2 (ACE-2) receptors may reduce the viral load in this group.[5,6]

The effect of the Waldeyer's lymphatic ring at the entry point of respiratory pathogens has essential functions in forming the immune response in childhood, and its effect on the frequency and severity of Covid 19 disease is not clearly known. The pharyngeal tonsil, which is a part of Waldeyer's ring, is very important in forming an effective immune response with predominantly T lymphocytes (especially CD8 T lymphocytes) and the effective antiviral cytokines especially interferon-alpha (IFN-a). It also contributes to mucosal immunity with secretory IgA, IgM, and IgG released from leukocytes on its mucosal surface. Palatine tonsils, another part of Waldeyer's ring, are also Mucosa Associated Lymphoid Tissue (MALT) related secondary lymphoid organs showing B and T cell activity.[7] While the function of adenoid and tonsil tissue is more prominent between the ages of 4-7, they start to regress from the adolescence period.[8]

Adenotonsillectomy (AT) is the most performed otorhinolaryngologic surgery in childhood because of obstructive hypertrophy and/or recurrent infections of the upper respiratory tract. Nevertheless, studies examining the effect of adenotonsillectomy on Covid-19 are very limited. This study investigated the incidence and severity of Covid-19 in the pediatric population undergoing adenotonsillectomy by conducting a comparative analysis with a control group, marking the inaugural comparison of its kind in the literature.

Methods

This retrospective study protocol was approved by the Ethics Committee of Sakarya University Faculty of Medicine (No: 74624) and was conducted in full accordance with the Declaration of Helsinki and Turkish laws and regulations. The files of patients aged 3-15 years who underwent AT between 2010 and 2020 in Sakarya University Faculty of Medicine, Ear Nose and Throat Clinic were scanned retrospectively. The AT group was formed by excluding the patients who did not have at least one year after the adenotonsillectomy operation, patients with missing or incorrect contact information, and patients with any autoimmune or hematological comorbidity. Subsequently, individuals with similar age and gender characteristics to the AT group, who presented to our clinic during the same period with diagnoses such as general examinations, nasal fractures, ear and hearing examinations, lymphadenitis, etc., and who had no history of AT, no diagnosis of immunodeficiency or hematological diseases, and complete contact information, were selected as the control (C) group. After the study and control groups were formed, the Covid-19 reverse transcription-polymerase chain reaction (rRT-PCR) test results of all participants included in the study were evaluated via the Public Health Management System (HSYS) for comparison.

All individuals testing positive on the rRT-PCR test were assessed based on their findings and symptoms, categorized into mild, moderate, severe, and critical disease as outlined in the World Health Organization's clinical management guide for Covid-19 (https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1), last updated on January, 2021. Subsequently, patients who underwent thoracic computed tomography (CT) imaging were radiologically evaluated for disease severity using the classification system established by Kunwei and colleagues.[9]

IBM SPSS version 26.0 for Windows statistical software (IBM Corporation, Armonk, New York, USA) was utilized for statistical analysis. Mean ± standard deviation represented continuous variables, while categorical variables were presented as percentages. Normality of distribution was assessed using Kolmogorov-Smirnov analysis, and non-parametric tests were favored based on the results. Mann-Whitney U test was employed for group-wise comparisons, and the Chi-square test was utilized for comparing categorical variables. Significance was established for p values less than 0.05.

Results

The files of 2089 patients who underwent AT in our clinic between January 2010 and January 2020 were reviewed retrospectively. As a consequence of this procedure, 286 patients were disqualified from the study due to not meeting the inclusion criteria. Out of the remaining 1803 patients, 804 (44.6%) were female; 999 (55.4%) were

males. The mean age in the AT group was 10.52 ± 2.89 (range 3-15 years). After the file scans of 1954 individuals, who could be considered the control group, 124 were found to be unsuitable and excluded from the study. Thus, a control group consisting of 1830 people was formed. The mean age in the control group was 10.95 ± 2.95 (range 3-15 years). 783 (42.8%) of the control group were women; 1047 (57.2%) of them were men. When comparing the groups based on age and gender data, no significant difference was observed between the two groups (p=0.505; p=0.17) (Table 1).

When the rRT-PCR test results for Covid-19 were analyzed for both groups, it was seen that 27 (1.5%) participants in the AT group were positive. In the control group, this rate was determined as 2.7% (50 participants). There was a statistically significant difference between the groups (p=0.001) (Table 1).

When the patients with positive test results were divided into groups according to the severity of disease, no patients were found to have a severe or critical disease, while 2 (7.4%) of the patients in the AT group and one (2%) of the patients in the C group had moderate complaints. The remaining patients of both groups experienced mild symptoms of Covid 19. The patients in both groups had no covid-19-associated multisystem inflammatory disease (MIS-C) illness with prolonged fever, abdominal pain, rash, hypotensive shock, and myocardial dysfunction.[10] No statistically significant difference was found between the groups in terms of disease severity (p=0.242) (Table 1).

Table 1. Demographics characteristics and RT-PCR positivity rates of the groups

		Adenotonsillectomy (n=1803)	Control (n=1830)	p
Gender	*Female*	804 (44.6%)	783 (42.8%)	0.17
	Male	999 (55.4%)	1047 (57.2%)	
Age		11[5]	11[5]	0.505
SARS-CoV-2 rRT – PCR test positivity rate		27 (1.5%)	50 (2.7%)	0.001*
WHO Classification	*Mild*	25 (92.6%)	49 (98.0%)	0.242
	Moderate	2 (7.4%)	1 (2.0%)	
	Severe	0%	0%	
	Critical	0%	0%	

Three patients in the AT group had positive rR-PCR test results and two in the C group had thorax CT imaging. When the semiquantitative visual total severity scores were evaluated, severity score was found as 1 in one patient in the control group, while it was found as 0 in the remaining four thoracic CT images. Since the number of thorax CTs images examined was few, the groups could not be compared statistically.

Discussion

The Waldeyer ring is a vital component of the immune system and plays a key role in countering bacterial and viral infections entering through the upper respiratory tract, with a particularly significant role in the pediatric population. Numerous studies report no long-term adverse effects of adenotonsillectomy on the immune system. However, conflicting evidence exists regarding its impact on respiratory tract infections.[8,11] Some studies suggest increased infections after adenotonsillectomy, while others indicate decreased.[12-14] Similarly, conflicting results have emerged regarding the relationship between adenotonsillectomy and COVID-19 outcomes.

Murugesan et al. reported a higher frequency of COVID-19 among individuals who had undergone adenotonsillectomy.[15] In contrast, a study conducted by our team in adult patients revealed a lower COVID-19 test positivity rate in the adenotonsillectomy group compared to controls (4% vs. 6.8%).[16] A large cohort study further supported these findings, suggesting that adenoidectomy and adenotonsillectomy may reduce the incidence of COVID-19.[17] The data presented in the present study similarly demonstrate a lower frequency of COVID-19 in pediatric cases that underwent surgery compared to those in a control group. This potential protective effect may be related to the dual role of lymphatic tissues of Waldeyer ring tissue. While they are integral to eliciting humoral and cellular immune responses, they can also serve as a reservoir for pathogens, potentially facilitating viral colonization and increasing infection risk.[7,18-20]

Pharyngeal and palatine tonsils are crucial for B cell activation and differentiation, triggering various immune responses, such as antibody production and complement activation.[21,22] During this process, it has been demonstrated that they secrete various pro-inflammatory and anti-inflammatory cytokines. The severe clinical symptoms of COVID-19, often linked to excessive cytokine production (cytokine storm), raise questions about whether Waldeyer's ring contributes to disease severity. By this pathophysiological process, the study of Chiang et al. indicated that mortality rates were lower in the tonsillectomy group.[23] However, other studies conducted by Kara et al. and Yang et al. concluded that tonsillectomy has no significant positive or negative effect on COVID-19 prognosis.[16,17] Our findings in this study are also consistent with those of these two studies. Nonetheless, further research is required to elucidate the precise mechanisms underlying these observations.

The presented study has some limitations. This single-center study design may limit the generalizability of findings. The study did not evaluate the procedure's effects in a fully healthy population without prior hospital admissions. Moreover, comparisons with larger, community-based cohorts were not conducted. However, a key strength of this study is its large pediatric sample size, which partially offsets these limitations.

In conclusion, our study contributes to the existing literature by demonstrating that adenotonsillectomy does not pose an additional risk for COVID-19 infection in the pediatric population. On the contrary, the incidence of COVID-19 was lower in individuals who underwent this procedure. Future studies involving larger, multicenter cohorts could investigate the potential effects of

adenotonsillectomy on multisystem inflammatory syndrome in children (MIS-C) and explore cytokine profiles during COVID-19 infection in this population.

Compliance with Ethical Standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The research protocol was submitted to and approved by the Sakarya University Ethics Committee. (25/20/2021 - 74624).

Conflict of Interest

The authors declare no conflicts of interest.

Author Contributions

The authors have contributed equally.

Financial Disclosure

None.

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