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Nazal Polipli Hastalarda COVID-19 İnsidansının ve Prognozunun Değerlendirilmesi

Evaluation of Incidence and Prognosis of COVID-19 in Patients with Nasal Polyps

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ÖZ

Amaç: Koronavirüs hastalığı 2019 (COVID-19), şiddetli akut solunum sendromu koronavirüs-2'nin (SARS-CoV-2) neden olduğu küresel bir pandemik bulaşıcı hastalıktır. IL -4, IL-5, IL-13 gibi tip 2 sitokinlerin ve eozionifililik enflamasyonun eşlik ettiği tip 2 immün yanıt nazal polipli kronik rinosinüzit (KRS+P) hastalarında COVID-19'a karşı potansiyel koruyucu etkisi olabilir. Bu çalışmada nazal polipli kronik rinosinüzit (KRS+P) hastalarında COVİD-19 sıklığı ve prognozu belirlemek amaçlandı.

Materyal ve Metot: KRS+P nedeniyle ameliyat edilen 15 -65 yaş arası hastalar, insidans ve hastalık şiddeti açısından kontrol grubu ile karşılaştırıldı.

Bulgular: KRS+P hastalarının %5,04'ünde Covid RT-PCR testi pozitif çıktı. Kontrol grubunda bu oran %8,96 idi ve her iki grup arasındaki fark istatistiksel olarak anlamlıydı. İki grup hastalık şiddeti açısından karşılaştırıldığında anlamlı bir fark bulunmadı.

Sonuç: KRS+P hastalarında COVID-19 insidansı daha düşüktü. Ancak nazal polip ile COVID-19 arasındaki ilişkiyi araştırmak için daha ileri prospektif çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: COVID-19, eozinofilik, insidans, nazal polip, sitokinler

ABSTRACT

Objective: Coronavirus disease 2019 (COVID-19) is a global pandemic infectious disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Type 2 immune response accompanied by type 2 cytokines such as IL-4, IL-5, IL-13, and eosinophilic inflammation, may have a potential protective effect against COVID-19 in chronic rhinosinusitis patients with nasal polyps (CRS + P). In the study, it was aimed to investigation the prevalence and prognosis of COVID-19 in chronic rhinosinusitis patients with nasal polyps (CRS + P).

Materials and Methods: Patients between the ages of 15-65 operated for CRS + P and were compared with the control group in terms of incidence and disease severity.

Results: Covid RT-PCR test was positive in 5.04% of CRS + P patients. This rate was 8.96% in the control group, and the difference between both groups was statistically significant. When the two groups were compared in terms of disease severity, no significant difference was found.

Conclusion: The incidence of COVID-19 was lower in patients with CRS + P. However, further prospective studies are needed to research the relationship between nasal polyp and COVID-19.

Keywords: COVID-19, cytokines, eosinophilic, incidence, nasal polyp

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INTRODUCTION

Chronic rhinosinusitis (CRS) is a common disease that affects 5.5 to 28% of the general population and is characterized by chronic inflammation in the sinonasal tissue.[1] CRS is classified clinically as CRS with nasal polyps (CRS + P) and CRS without nasal polyps (CRS-P). Studies have shown that there are various immunological mechanisms between patients with CRS + P and patients with CRS-P and, therefore, different endotypes could be defined.[2,3] The PRACTALL consensus report by the European Academy of Allergy and Clinical Immunology and the American Academy of Allergy, Asthma and Immunology summarizes CRS phenotypes and endotype information.[2] CRS + P endotypes are characterized by type 1, 2, and type 3 inflammatory endotypes according to the status of inflammatory cells, T helper cells, interleukins, and other cytokines. The most common pathway in CRS + P is the type 2 immune pathway (20 -87%).[4]

Coronavirus disease-2019, caused by the virus named severity acute respiratory syndrome Coronavirus 2 (SARS-CoV-2), was first reported in December 2019.[5] SARS-CoV-2 infections may be asymptomatic, but it usually affects the respiratory system, causing severe pneumonia, fever, cough and shortness of breath, acute respiratory distress syndrome, and even multiple organ failure.[6] Individuals with hypertension, obesity, diabetes, cardiovascular disease, chronic obstructive pulmonary disease, and the elderly are at greater risk of having severe COVID-19.[7] Interestingly, some studies have shown that the prevalence of COVID-19 is significantly lower in adult populations with asthma and allergic rhinitis patients.[7-9]

SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) receptor to enter the cell and TMPRSS2 (transmembrane serine protease 2) for S (spike) protein priming.[10,11] A recent study showed that the SARS-CoV-2 input gene ACE2 and TMPRSS2 are more common in the upper airway than in the lower airway.[12] Saheb Sharif-Askari et al.[13] showed in their prospective study that the number of ACE 2 and TMPRSS2 receptors were low in patients with nasal polyps in which the type 2 immune pathway was active. In addition, some type 2 cytokines such as IL-4, IL-13, and IL-9 also have anti-inflammatory effects.[14] For example, IL-4 can suppress the growth of Th0-activated Th1 cells and inhibit the production of multiple proinflammatory cytokines, including IL -1β, TNF-α, IL-6, and IL-12.[15,16]

In the study, we aimed to investigate the risk of COVID-19 infection in patients with chronic sinonasal inflammation with nasal polyps.

MATERIALS AND METHODS

Ethical Status: The research protocol was submitted to and approved by the Sakarya University Ethics Committee (Date: 16.04.2021, decision no: 256). It has been conducted according to Turkey country's laws and regulations and the ethical rules in the Declaration of Helsinki.

Studying Group: Seven hundred-thirteen patients were operated for CRS + P between January 2010 and January 2020 in our department. They were determined as the study group. The control group was composed of 747 patients who had no history of CRS and underwent only septoplasty operation. Patients with immunosuppressive, pregnancy status, fungal sinusitis, benign and malignant tumors were not included in the study. The COVID-19 PCR test results of all participants were evaluated through the Public Health Management System and compared between the two groups. Moreover, the count and percentage of eosinophils in the hemogram of both groups were analyzed and compared.

Study and Evaluations: All of the COVID-19 positive cases were evaluated according to their findings and symptoms. It was classified as a mild, moderate, severe, and critical disease according to the World Health Organization's clinical management guidelines for COVID-19, updated on January 25, 2021. According to this classification, mild clinical symptoms without pneumonia in imaging were determined as mild type; fever, respiratory tract, and other symptoms with pneumonia in imaging were determined as moderate type; respiratory distress, respiratory rate ≥ 30 times/min; in resting state, oxygen saturation ≤ 93%; PaO2 / FiO2 300mmHg were determined as severe type; respiratory failure requiring mechanical ventilation, shock and other organ failure requiring intensive care unit monitoring and treatment were determined as critical type.

In addition, patients with chest computed tomography (CT) were classified radiologically in terms of disease severity. According to Li et al.[17], the percentage of involvement in the whole lobe of both lungs and the overall lung total severity score (TSS) were recorded. Each of the five lung lobes was evaluated in terms of lobar involvement. It was classified as none (0%), minimal (1-25%), mild (26-50%), moderate (51-75%) or severe (76-100%).

Later, according to these involvement percentages, it was scored as 0, 1, 2, 3, or 4. The TSS was reached by aggregate the five lobe scores (range from 0 to 20).

Statistical Analysis: Statistical analysis was performed using IBM SPSS version 22.0 for Windows statistical software (IBM Corporation, Armonk, New York, USA). Continuous variables were expressed as mean ± standard deviation and categorical variables were expressed in percentage. Kolmogorov -Smirnov analysis was performed for distribution normality analyzes. Non-parametric tests were preferred according to the results of this analysis. An independent sample t-test was used for the pairwise comparisons between groups. Chi-square test was used for the comparison of the categorical variables. P values less than 0.05 were accepted as significant.

RESULTS

In the CRS + P group (491 (68%) male, 222 (32%) female), the mean age was 42.99 ± 13.03 years (range 15-65 years). The control group consisted of 386 (51.67%) female and 361 (48.3%) male with a mean age of 33.68 ± 9.94 years (range 15-65 years). The demographic characteristics of the groups are compared in Table 1.

In the CRS + P group, 36 (5.04%) patients were positive for the PCR test. This rate is 8.96% (67 patients) in the control group. A statistically significant difference was found between the two groups in terms of PCR test positivity (p= 0.003). When the two groups were compared in terms of eosinophil count and percentage, a significant difference was found (p <0.001). In terms of the severity of disease and the lung TSS, the PCR positive patients were analyzed between the study and the control groups, the differences were not statistically significant (p = 0.073, p = 0.205, respectively) (Table 1).

Moreover, the patients were divided as PCR positive and negative in the study group and compared in terms of eosinophil count and percentage, a significant difference was not observed (p = 0.886; 0.915, respectively) (Table 2).

DISCUSSION AND CONCLUSION

The present study showed that the prevalence of COVID-19 was lower in patients with CRS + P. These findings are consistent with the knowledge that cytokines and eosinophilic inflammation have a protective effect against COVID-19 infection. The cytokines related to type 2 inflammation, such as IL-4, IL-5, and IL-13 may be reduced ACE2 expression in the nasal mucosa of CRS +P patients.[13,18]

In this period when the spread of COVID-19 continues worldwide, it becomes important to identify potential risk factors to reduce the transmission of

Table 1. The demographic characteristics and clinical data of all patients.

		The Study Group (n=713)	**The Control Group (n=747)**	**p**
Gender (n/%)	Female	222 (%32)	386 (%51.67)	**<0.001**
	Male	491 (%68)	361 (%48.3)	
Age (mean±SD)		42.99 ± 13.03	33.68 ± 9.94	**<0.001**
Positivity of PCR test (n/%)		36 (% 5.04)	67 (%8.96)	**0.003**
Eosinophil count (K / uL)		0.37 ± 0.28	0.17 ± 0.15	**<0.001**
Percentage of eosinophils		%4.52 ± 3.47	%2.33 ± 2.08	**<0.001**
WHO Classification	Mild	30 (%83.3)	63 (%94.02)	0.073
	Moderate	4 (%11.1)	4 (%5.97)	
	Severe	1 (%2.7)	0 (%0)	
	Critical	1 (%2.7)	0 (%0)	
Chest CT		9 / 36	19 / 67	0.715
TSS		1.77 ± 2.72	1 ± 3.34	0.205

CT: Computerized Tomography; TSS: Total Severity Score; SD: Standard Deviation; Bold values indicate significance (p<0.05).

Table 2. The count and percentage of eosinophilia in the CRS + P patients with COVID + and COVID –.

	CRS + P with COVID +	**CRS + P with COVID -**	**p**
Eosinophil count (K / uL)	0.38 ± 0.29	0.38 ± 0.29	0.886
Percentage of eosinophils	4.48 ± 3.9	4.54 ± 3.2	0.915

COVID-19 disease and improve prognosis. While hypertension, obesity, diabetes, cardiovascular disease, chronic obstructive pulmonary disease are considered risk factors for COVID-19. The frequency of COVID-19 is lower in asthma, and other respiratory allergic diseases with less ACE2 count, and these diseases have been stated as protective factors.[7,19] Saheb Sharif-Askari et al.[13] stated that patients with CRS + P are at lower risk for COVID-19 due to the low level of the SARS-CoV-2 input gene, ACE2, and TMPRSS2. The data in our study supports this view, showing that patients with CRS + P have a lower incidence of COVID-19.

In the previous study, patients with CRS + P were classified as eosinophilic CRS + P, and non-eosinophilic CRS + P. Moreover, histopathologically ACE2 and TMPRSS2 genes and cytokines were compared. IL-4, IL-5, IL-13 were found to be significantly higher and ACE2 and TMPRSS2 were found to be significantly lower in patients with eosinophilic CRS + P.[13] In our study, although the eosinophil value was found to be significantly higher in the CRS + P compared to the control group, no significant difference was found between PCR positive and negative patients in the group with CRS + P.

Nasal or systemic steroids are the first treatment options to reduce nasal symptoms and improve patients' quality of life by reducing the size of nasal polyps. Steroids act by regulating the immune response and suppressing inflammation.[20] Wang et al.[21] found that ACE 2 receptors decreased significantly in the non-eosinophilic CRS group after steroid treatment and stated that this decrease was due to the inhibitory effects of steroids in the type 1 pathway.

In our study, the severity of the Covid-19 disease in patients with CRS + P was determined radiologically and clinically. Chronic diseases such as hypertension, obesity, diabetes, cardiovascular disease, chronic obstructive pulmonary disease are risk factors for having COVID-19 and the severity of the disease.[18] We determined that the incidence of COVID-19 is low and did not negatively affect the severity of COVID-19 in the patients with CRS + P.

In the study by Yang et al.[22], pneumonia was present in all 41 infected cases in Wuhan. In another study, patients without signs of pneumonia were shown to be PCR positive.[6] However, chest CT is expected to guide the treatment and evaluate the clinical severity correctly and combine with clinical information rather than being used in diagnosis alone.[17] There were 30 (83.3%) mild cases in our study without signs of pneumonia in chest CT among 36 COVID-19 patients in the CRS + P group. However, TSS was relatively higher but not statistically significant in the study group.

In conclusion, one of the few limitations in our study is that firstly, CRS endotype profile cannot be examined since eosinophilia and cytokines such as IL-4, IL5, IL13, IFN-γ, IL17 cannot be analyzed in the histopathology of patients with CRS + P. Secondly since PCR positivity is checked among the patients with COVID-19 complaints, the PCR positivity rate may be relatively high. However, we do not think that it creates a systematic error since both groups were observed in the same way. The present study observed that the incidence of COVID-19 was lower in patients with CRS + P. In addition, we showed that CRS + P does not have a negative effect on the severity of COVID-19 disease clinically and radiologically.

To our knowledge, the impact of allergic inflammation, nasal polyposis or chronic nasal mucosal infection on the level of expression of ACE2 and TMPRSS2 is still not fully understood. In our study, the incidence of COVID-19 was lower in patients with CRS + P, however, the reason for this may be the underlying factors causing nasal polyp development and we think that it may be a mechanism that reduces the attachment of the virus in the nose and its entry into the body. Comprehensive scientific studies are needed on this subject.

Ethics Committee Approval: The research protocol was submitted to and approved by the Sakarya University Ethics Committee (Date: 16.04.2021, decision no: 256).

Conflict of Interest: No conflict of interest was declared by the authors.

Author Contributions: Concept – Nİ, DD; Supervision – DD, MG; Materials – Nİ, KD; Data Collection and/or Processing – Nİ, DD, KD; Analysis and/ or Interpretation – MG, MSY, AK; Writing –Nİ, DD.

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