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Risk Factors and Comorbidities of Recurrent Nasal Polyposis

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ABSTRACT

Chronic rhinosinusitis is divided into two groups, which are Chronic rhinosinusitis with nasal polyps (CRSwNP) and without nasal polyps (CRSsNP). The rate of post-surgical recurrence in the CRSwNP is high, and predicting factors are unknown. This study aims to identify and evaluate risk factors associated with treatment-resistant and recurrent CRSwNP.

This cross-sectional study evaluates demographic data and atopic risk factors in patients with CRSwNP, including a high IgE level (≥100 U/mL), skin prick test (SPT) for aeroallergens, aspirin-exacerbated respiratory disease (AERD), and asthma prevalence. An oral aspirin challenge was performed to diagnose AERD. 191 patients with CRSwNP were enrolled, with 73 patients in the recurrent, and 118 patients in the non-recurrent group. The mean age of the patients in the recurrent group was 45.08±12.05. The mean age of the patients in the non-recurrent group was 42.89±11.73. 49. Asthma prevalence in recurrent- CRSwNP is significantly higher than non-recurrent CRSwNP Asthma severity in recurrent CRSwNP and AERD patients was significantly higher than in nonrecurrent CRSwNP and non-AERD patients. The level of IgE in the recurrent- CRSwNP is higher than non-recurrent CRSwNP. Positive SPT results for tree, weed, and mite allergens were higher in the non-recurrent- CRSwNP group compared to the recurrent CRSwNPgroup.

Asthma had a significantly higher difference in AERD compared to non-AERD. The level of IgE in AERD is higher than non-AERD.

Recurrent CRSwNP patients and AERD patients had Higher IgE levels. Asthma is more prevalent and more severe in both AERD and recurrent CRSwNP. However, a positive SPT result has been seen higher in non-recurrent CRSwNP.

Keywords: Aspirin-exacerbated respiratory disease; Chronic rhinosinusitis with nasal polyps; Recurrent nasal polyposis; Skin prick test

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INTRODUCTION

Chronic rhinosinusitis (CRS) is characterized by the presence of mucosal inflammation in the nasal cavity and paranasal sinuses for more than three months.[1] CRS

can be classified into two distinct groups based on the presence or absence of nasal polyps: Chronic rhinosinusitis with nasal polyps (CRSwNP) and Chronic rhinosinusitis without nasal polyps (CRSsNP). Nasal polyposis does not have a definite etiology, and different inflammatory pathways have a role in the pathophysiology of the disease, such as type 1 and type 2 inflammation, increasing levels of IL-13, and eosinophilia.[2,3] Nasal polyps are more prevalent in patients with persistent asthma, aspirin-exacerbated respiratory disease (AERD), and cystic fibrosis.[4] CRSwNP with associated asthma has a unique characteristic, which is the presence of tissue eosinophilia and elevated local IgE levels. Moreover, Local IgE levels are polyclonal and functional and increase in polyps regardless of serum IgE and atopic status. In nasal polyps, IgE generation is triggered by both allergens and *Staphylococcus aureus* colonization.[5] Individuals with both CRSwNP and asthma have more severe sinonasal symptoms and often have more challenging treatment. Standard medical management for CRSwNP typically includes regular nasal saline irrigations and the use of intranasal steroids. Systemic corticosteroids and antibiotics are used during exacerbations of the disease.[6] In cases in which CRSwNP is resistant to medical treatment, multiple surgical interventions and additional adjuvant medical therapy may be necessary.[6,7] Recent studies have shown that biological drugs, including omalizumab and dupilumab, have a role in the treatment of recurrent CRSwNP and individuals with recent sinus surgeries.[8]

The recurrence of nasal polyposis has been reported in 20-60% of patients; however, the precise predicting factors for recurrence are not entirely understood.[9] However, Recent studies suggested that eosinophil density, interleukin-5, asthma, and the presence of anti-ds-DNA can be the predicting factor for nasal polyposis recurrence.[10] Recent studies discussed the role of age, genetics, and eosinophilia in the recurrence of nasal polyposis.[11]

Considering the pathogenesis underlying the recurrence of nasal polyposis, a strong association can be assumed between allergies and the recurrence of nasal polyps.[12] Multiple studies observed the role of IgE in the pathogenesis of nasal polyposis. Functionally active IgE is detected in the nasal polyp mucosa, capable of activating mast cells. Skin prick testing (SPT) is a diagnostic procedure for confirming sensitization in IgE-mediated diseases, including asthma, rhino-conjunctivitis, eczema, and anaphylaxis.[13] Nasal polyps with a predominance of eosinophils are more common in patients with AERD. Given the prominent role of allergy and IgE in the pathophysiology of the disease, conducting an SPT can be a valuable tool in identifying the allergic phenotype and allergic rhinitis in patients.[14] Furthermore, specific IgE antibodies are identified within nasal polyp tissue independently of their presence in the serum. The efficacy of anti-IgE therapy in individuals with nasal polyposis further supports the involvement of IgE in the disease.[15]

Aspirin-exacerbated respiratory disease (AERD) is defined by persistent nasal polyposis, eosinophilic chronic sinusitis, asthma, and adverse reactions to nonsteroidal anti-inflammatory drugs (NSAIDs). AERD has been diagnosed in 8% to 26% of patients with CRSwNP and 10% to 20% of patients with asthma.[16] While a hypersensitivity to NSAIDs can occur before the respiratory disease, most patients experience the onset of asthma and CRSwNP before experiencing NSAID reactions at a later stage of the disease progression.[17] Individuals with AERD should be evaluated for asthma, sinonasal polyposis, and aspirin sensitivity. Thus, the objective of this research is to assess the levels of IgE, and eosinophil counts, perform SPT, and investigate the prevalence of AERD and asthma in individuals with recurrent and non-recurrent nasal polyposis. This study aims to identify the potential risk factors associated with recurrent CRSwNP.

MATERIALS AND METHODS

Study Design

This cross-sectional study was conducted in 2022-2023. The present study is designed to evaluate IgE level, and SPT for aeroallergens, AERD, and asthma prevalence in patients with recurrent and non-recurrent CRSwNP. In this study, clinical data were collected from patients above 18 years old who were referred to an immunology clinic in Shiraz, Iran. The sampling method is census sampling, and a total of 191 patients were enrolled in the study.

Data Gathering

All the cases in this study were evaluated by allergy and clinical immunology subspecialists. Data of these patients were collected from a complete history, physical examination and lab work-up, and skin prick testing and documented on a data sheet. Demographic

characteristics of the patients are age, and sex (male or female). Other data are frequency of polyp surgeries, asthma and history of reflux, having AERD and level of IgE (U/mL), and also the skin prick test result was collected. SPT results are indoor and outdoor aeroallergens (grass pollens -weed pollens-tree pollens as outdoor aeroallergens, and mite-molds are indoor aeroallergens). The level of IgE in this study was divided into two distinct groups (IgE below 100 U/mL and above 100 U/mL, which is considered high IgE). An oral aspirin challenge test in two days was used to diagnose AERD patients according to the Nabavi et al, study, which performed this test.[16] After that, the patients were divided into AERD and non-AERD groups. A history of previous polyp surgeries was obtained in which the patients with two or more surgeries were considered Recurrent nasal polyposis, and patients with one or fewer surgeries considered nonrecurrent nasal polyposis. All the data are confidential. All of the patients had informed consent, and the ethics committee of the Shiraz University of Medical Sciences approved this study. (IR. SUMS. MED.REC.1401.184)

Inclusion and Exclusion Criteria

Inclusion criteria are all of the patients who have been referred to an immunology clinic with CRSwNP. These patients were divided into recurrent and non-recurrent subgroups regarding the surgery and treatment history. Patients were eligible for inclusion if a minimum of one year had elapsed since their initial surgery.

The exclusion criteria encompassed patient withdrawal from the study, contraindications to skin prick tests, and diagnoses other than chronic rhinosinusitis and nasal polyposis. Additionally, patients who had used systemic corticosteroids and antibiotics within 30 days of examination were excluded.

Statistics

Classified variables were reported as percentage and frequency. The demographic information of the patients will be reported using the mean and standard deviation for the quantitative data and also the frequency and percentage for the qualitative data. The chi-square test was used to compare the differences and related risk factors, including Asthma, IgE level, GERD, and skin prick test results between the recurrent and non-recurrent nasal polyposis groups and also will be used to compare those variables in AERD and Non-AERD groups. The chi-square was used to Compare other variables in the other groups provided in Table 3-4. *p* values below 0.05 were considered statistically significant. All analyses were conducted using IBM SPSS software for Windows version 28. The tables were generated using Microsoft Word and Excel 2019.

RESULTS

A total of 191 patients with nasal polyps referred to the immunology clinic were enrolled in the study. Subsequently, 73 patients were evaluated in the recurrent CRSwNP group and 118 patients in the non-recurrent group. The mean age of the patients participating in the recurrent CRSwNP group was 45.08±12.05. The mean age of the patients participating in the non-recurrent CRSwNP group was 42.89±11.73. 49 (%67.1) of 73 patients in the recurrent CRSwNP group were male, and 24 (%32.9) of the patients in the mentioned group were female. 63 (%53.4) out of 118 patients in the non-recurrent group were male, and 55 (%46.6) of these patients were female. According to the results in Table 1, there was no significant difference in age and gender between the patients in the two study groups ($p>0.05$). (Table 1)

Based on the findings in Table 1, the prevalence of asthma among recurrent CRSwNP patients was significantly higher compared to non-recurrent patients ($p=0.017$).).

The study results indicate that 43% of patients with two or more recurrences of CRSwNP had severe asthma, whereas this percentage was 16% for those with less than two recurrences and 1% for patients without any recurrence. This finding suggested a significantly higher severity of asthma with a higher recurrence rate of CRSwNP ($p=0.005$). According to the results in Table 1, the level of IgE in the recurrent- CRSwNP patients is significantly higher than 100U/mL compared to non-recurrent patients ($p=0.041$). There was no significant difference in the presence of AERD between the patients in the two study groups (recurrent and non-recurrent groups) ($p=0.331$). Additionally, positive SPT results for tree, weed, and mite allergens were significantly lower in the recurrent- CRSwNP patients compared to the non-recurrent CRSwNP patients ($p<0.05$).

Table 1. Comparison of Demographic data and risk factors between Recurrent and Non-Recurrent CRSwNP patients

Variable		Study Groups (All patients)		*p*
		Recurrent CRSwNP	Non-Recurrent CRSwNP	
Age Mean±SD		45.08±12.05	42.89±11.73	0.246
Sex, N (%)				
	Male	49 (%67.1)	63 (%53.4)	**0.07**
	Female	24 (%32.9)	55 (%46.6)	
Asthma, N (%)				
	YES	54 (%74)	67 (%56.8)	**0.017**
	NO	19 (%26)	51 (%43.2)	
AERD, N (%)				
	YES	25 (% 34.2)	32 (% 27.1)	0.331
	NO	48 (%65.8)	86 (%72.9)	
GERD, N (%)				
	YES	10 (%13.7)	22 (%18.6)	0.429
	NO	63 (% 86.3)	96 (% 81.4)	
IgE level, N (%)				
	≥ 100 U/mL	52 (% 71.2)	66 (% 56.4)	**0.041**
	<100 U/mL	21 (%28.8)	51(% 43.6)	
IgE level, Mean±SD (U/mL)		303.91±247.73	287.48±230.6	0.461
Skin prick test results, N (%)	**Tree**			
	positive	10 (%13.7)	48 (%40.7)	**<0.001**
	negative	63 (%86.3)	70 (%59.3)	
	Weed			
	positive	21 (%28.8)	52 (%44.1)	**0.034**
	negative	52 (%71.2)	66 (%55.9)	
	Grass			
	positive	16 (%21.9)	37 (%31.4)	0.185
	negative	57 (%78.1)	81 (%68.6)	
	Mite			
	positive	5 (%6.8)	26 (%22)	**0.006**
	negative	68 (%93.2)	92 (%78)	
	Mold			
	positive	4 (%5.5)	11 (%9.3)	0.415
	negative	69 (%94.5)	107 (%90.7)	

GERD: Gastroesophageal reflux disease, AERD: Aspirin-exacerbated respiratory disease, CRSwNP: Chronic rhinosinusitis with nasal polyps, IgE: Immunoglobulin E

According to the results in Table 2, 57 patients (%28.1) were classified under the AERD group, and 134 (%71.9) were categorized in the non-AERD group. The mean age of the patients in the AERD group was 44.42±11.71. The mean age of the patients in the non-AERD group was 43.44±11.98. 28 (%49.1) of 57 patients in the AERD group were male, and 29 (%50.9) of 57 patients were female. Whereas, 84 (%62.7) of 134 patients in the non-AERD group were male, and 50 (%37.3) of these patients were female. As shown in Table 2, no significant difference was found in age and gender between the patients in the AERD and non-AERD groups ($p>0.05$). Furthermore, no difference was indicated in the number of previous nasal polyp surgeries between the AERD and non-AERD groups ($P=0.445$). Asthma in AERD patients was more significant than in non-AERD patients ($p=0.024$). As shown in Table 5, 50% of AERD patients had experienced severe asthma, while only 1% of non-AERD patients had severe asthma. Additionally, the majority of non-AERD patients (40%) did not experience asthma at all. Among AERD patients who had CRSwNp recurrence of ≥2, the incidence rate of severe asthma was 50%, whereas it was 14% in AERD patients who had CRSwNp recurrence less than 2 times. Overall, asthma was significantly more prevalent with higher severity in AERD patients compared to non-AERD patients, and more recurrence was associated with higher severity of asthma ($p=0.001$) (Table 7). The level of IgE in AERD patients was significantly higher than 100U/mL compared to non-AERD patients ($p=0.005$) (Table 2). Moreover, the level of IgE in patients with recurrent CRSwNP and AERD was significantly higher than 100 U/mL compared to the patients with recurrent CRSwNP and non-AERD (Table 3). There was no difference in the skin prick test results for tree, weed, grass, mite, and mold allergens between the AERD and non-AERD patients ($p>0.05$). However, weed was the most prevalent allergen in the AERD and non-AERD (Table 2).

As indicated in Table 4, no statistically significant age difference was found between the recurrent and non-recurrent patients with AERD ($p>0.05$). However, there was a significant difference between those two groups; the male gender is higher in AERD with recurrent CRSwNP ($p<0.05$). GERD history was not statistically meaningful in all groups of the study ($p>0.05$). Notably, weed pollen was the most common allergen in all groups of the study (Tables 1-4).

The results indicated that a high plasma eosinophil count (more than 500 cells per mL) was seen in 12% of CRAwNP patients who had≥2 recurrences. This percentage was reported as 7% and 6% in patients with less than 2 recurrences and non-recurrent CRSwNP patients, respectively. However, the higher eosinophil count in CRAwNP patients who had ≥2 recurrences was not statistically significant in our study ($p=0.42$). As mentioned in Table 5, a high plasma eosinophil count was observed in 12% of AERD patients and 8% of Non-AERD patients. However, the impact of AERD, like the recurrence of CRSwNP, did not show a statistically significant effect on higher plasma eosinophil levels.

Using multivariate regression analysis to investigate the effect of different basic and clinical factors on diabetes complications, we showed significant effects of CD4+CD25+FoxP3+Helios+ Tregs on UACR (P=0.034) in the presence of diastolic blood pressure, HDL and HbA1C; CD4+CD25+FoxP3+Helios+ NRP-1+ Tregs on CIMT ($p=0.05$); CD4+CD25+FoxP3+Helios+ Tregs ($p=0.012$) and CD4+CD25+FoxP3+Helios- Tregs ($p=0.033$) on HbA1c in the presence of TG ($p=0.011$) and Hct ($p=0.002$; data not shown).

Table 2. Comparison of Demographic data and risk factors between AERD and Non-AERD Patients

Variable		Study Groups (All patients)		*p*
		AERD	Non-AERD	
Age Mean±SD		44.42±11.71	43.44±11.98	0.246
Sex, N (%)				
Male		28 (%49.1)	84 (%62.7)	0.108
Female		29 (%50.9)	50 (%37.3)	
Asthma, N (%)				
YES		43 (%75.4)	78 (%58.2)	**0.024**
NO		14 (%24.6)	56 (%41.8)	
GERD, N (%)				
YES		8 (%14)	24 (%17.9)	0.672
NO		49 (%86)	110 (%82.1)	
IgE level, N (%)				
≥ 100 U/mL		44 (%77.2)	74 (%55.6)	**0.005**
<100 U/mL		13 (%22.8)	59 (%44.4)	
IgE level, Mean±SD (U/mL)		325.8±314.05	272.82±204.24	0.757
Number of Polyp surgery Mean±SD		1.56±1.46	1.35±1.19	0.445
Skin prick test results, N (%)	**Tree**			
	positive	18 (%31.6)	40 (%29.9)	0.864
	negative	39 (%68.4)	93 (%70.1)	
	Weed			
	positive	23 (%40.4)	50 (%37.3)	0.746
	negative	34 (%59.6)	84 (%62.7)	
	Grass			
	positive	15 (%26.3)	38 (%28.4)	0.861
	negative	42 (%73.7)	96 (%71.6)	
	mite			
	positive	8 (%14)	23 (%17.2)	0.672
	negative	49 (%86)	111 (%82.8)	
	mould			
	positive	4 (%7)	11 (%8.2)	0.779
	negative	53 (%93)	123 (%91.8)	

GERD: Gastroesophageal reflux disease; AERD: Aspirin-exacerbated respiratory disease; CRSwNP: Chronic rhinosinusitis with nasal polyps; IgE: Immunoglobulin E

Table 3. Comparison of Demographic data and risk factors between AERD with Recurrent CRSwNP and Non-AERD with Recurrent CRSwNP Patients

Variable		Study Groups (Patients with Recurrent-CRSwNP)		*p*
		AERD	Non-AERD	
Age Mean±SD		46.92±11.78	44.12±12.19	0.351
Sex, N (%)		17 (%68)	32 (%66.7)	0.9
Male		8 (%32)	16 (%33.3)	
Female				
Asthma, N (%)		22 (%88)	32 (%66.7)	0.055
YES		3 (%12)	16 (%33.3)	
NO				
GERD, N (%)		3 (%12)	7 (%14.6)	0.761
YES		22 (%88)	41 (%85.4)	
NO				
IgE level, N (%)		20 (%80)	32 (%66.7)	**0.013**
≥ 100 U/mL		5 (%20)	16 (%33.3)	
<100 U/mL				
IgE level, Mean±SD (U/mL)		409.4±371.28	208.7±183.39	0.284
Number of Polyp surgery Mean±SD		2.8±1.35	2.64±0.95	0.952
Skin prick test results, N (%)	**Tree**	3 (%12)	7 (%14.6)	0.761
	positive	22 (%88)	41 (%85.4)	
	negative			
	Weed	8 (%32)	13 (%27.1)	0.66
	positive	17 (%68)	35 (%72.9)	
	negative			
	Grass	6 (%24)	10 (%20.8)	0.756
	positive	19 (%76)	38 (%79.2)	
	negative			
	mite	2 (%8)	3 (%6.3)	0.779
	positive	23 (%92)	45 (%93.8)	
	negative			
	mold	1 (%4)	3 (%6.3)	0.689
	positive	24 (%96)	45 (%93.8)	
	negative			

GERD: Gastroesophageal reflux disease; AERD: Aspirin-exacerbated respiratory disease; CRSwNP: Chronic rhinosinusitis with nasal polyps; IgE: Immunoglobulin E

Table 4. Comparison of Demographic data and risk factors between Recurrent CRSwNP with AERD and Non-Recurrent CRSwNP with AERD Patients

Variable		Study Groups (patients with AERD)		*p*
		Recurrent CRSwNP	Non-Recurrent CRSwNP	
Age Mean±SD		46.92±11.78	42.46±11.46	0.212
Sex, N (%)		17 (%68)	11 (%34.4)	**0.017**
Male		8 (%32)	21 (%65.6)	
Female				
Asthma, N (%)		22 (%88)	21 (%65.6)	0.067
YES		3 (%12)	11 (%34.4)	
NO				
GERD, N (%)		3 (%12)	5 (%15.6)	0.696
YES		22 (%88)	27 (%84.4)	
NO				
IgE level, Mean±SD (U/mL)		409.4±371.28	269.34±239.34	0.398
Skin prick test results, N (%)	**Tree**	3 (%12)	15 (%26.3)	**0.009**
	positive	22 (%88)	17 (%53.1)	
	negative			
	Weed	8 (%32)	15 (%46.9)	0.289
	positive	17 (%68)	17 (%53.1)	
	negative			
	Grass	6 (%24)	9 (%28.1)	0.771
	positive	19 (%76)	23 (%71.9)	
	negative			
	Mite	2 (%8)	6 (%18.8)	0.444
	positive	23 (%92)	26 (%81.3)	
	negative			
	Mold	1 (%4)	3 (%9.4)	0.623
	positive	24 (%96)	29 (%90.6)	
	negative			

GERD: Gastroesophageal reflux disease; AERD: Aspirin-exacerbated respiratory disease; CRSwNP: Chronic rhinosinusitis with nasal polyps; IgE: Immunoglobulin E

Table 5. The correlation between AERD and the severity of asthma.

variable		AERD		Non-AERD (n:134)	*p*
		CRSwNp recurrence. N≥2, (n:18)	CrSwNp recurrence. N<2, (n:7)		
Asthma positive (Severity)	**Severe persistent**	9(50%)	1(14%)	1(1%)	0.001
	Moderate persistent	5(28%)	2(28%)	15(11%)	
	Mild persistent	3(16%)	1(14%%)	22(16%)	
	Intermittent	0	1(14%)	40(30%)	
Asthma negative		1(5%)	2(28%)	56(41%)	

AERD: Aspirin-exacerbated respiratory disease; Recurrence N: Recurrence number; CRSwNP: Chronic rhinosinusitis with nasal polyps

DISCUSSION

CRSwNP is a chronic condition that affects the nasal cavity and sinuses. CRSwNP has a high recurrence rate. Local IgE is polyclonal and its levels increase in polyps regardless of serum IgE and atopic status. In nasal polyps, IgE generation is triggered by both allergens and Staphylococcus aureus colonization.[5] In some cases, a combination of medical and surgical interventions may be required to manage CRSwNP effectively.[6] In this cross-sectional study, IgE level, AERD, asthma, skin prick test results, and GERD history were evaluated in the CRSwNP patients. The prevalence of AERD in the current study was %29.8 among patients with CRSwNP, which is slightly higher than the previous studies.[16] However, the overall prevalence of AERD in the general population is around 0.3 to 2.5 percent.[18] Nevertheless, in another study, among patients with CRSwNP, the prevalence of AERD was found to be 16%. AERD is a frequently observed condition among patients who have CRSwNP and Asthma.[19] A study by Nabavi et al, in 2014 suggested that in CRSwNP, A.S.A. hypersensitivity was more common, and the prevalence of AERD among CRSwNP was 48.8%. Furthermore, these patients should be evaluated for AERD and its progression. Therefore, to diagnose AERD, the oral aspirin challenge test should be done in the patients and history was not sufficient for the diagnosis.[16] These differences in the prevalence of AERD among CRSwNP could be due to racial and genetic differences. Esmaeilzadeh et al revealed two HLA variations that were associated with AERD and highlighted the role of genetics in the disease.[20] Most of the participants with CRSwNP are male patients, with %58.6 of the study population. This is consistent with a previous systematic review study in which CRSwNP is more common in male patients (%59.8).[21]

Complete recurrence risk factors of CRSwNP have not been understood yet. However, a recent study demonstrated risk factors for the recurrence of CRSwNP. These risk factors include Asthma, genetic variations, age, and eosinophilia. These factors have been reported as potential contributors to the likelihood of polyp regrowth and CRS recurrence. Asthma, in particular, has been identified as a significant risk factor.[11,22] In the current study, asthma is found to be associated with patients with recurrent CRSwNP compared to those with non-recurrent CRSwNP. Furthermore, as indicated in our study, higher recurrence has been associated with a greater prevalence and increased severity of asthma. These findings are consistent with similar research linking asthma to CRSwNP, suggesting that patients with CRSwNP exhibiting type-2 inflammation may face a more challenging clinical course, experiencing more severe asthma, a higher likelihood of recurrent nasal polyps, and a greater prevalence of asthma.[23] The prevalence of uncontrolled asthma in patients with AERD is considerably high, with a rate of 45.3%. In our research, asthma was found to be more strongly associated with AERD compared to the non-AERD group. Additionally, our study revealed that AERD patients experienced higher asthma severity compared to non-AERD patients. Among AERD patients, there was a correlation between higher severity and prevalence of asthma and an increased recurrence of CRSwNP. Specifically, asthma severity showed a direct relationship with CRSwNP recurrence. This has been observed in various

populations of individuals with asthma.[24] Notably, patients with recurrent CRSwNP were more associated with asthma than non-recurrent CRSwNP. This finding shows that asthma can be associated with more recurrence in CRSwNP and can be defined as a predictor of recurrence in this disease.[10] Another study revealed the risk factors for recurrent surgery in CRS. These factors include allergic rhinitis, corticosteroid treatment, and previous CRS surgery.[25]

In the current study, we did not observe a significant correlation between a high plasma eosinophil count and the recurrence of CRSwNP. Additionally, we did not find a significant relationship between a high eosinophil count and AERD. In literature, it has been reported that a higher recurrence rate of CRSwNP is linked to elevated eosinophil counts.[21] However, our findings showed no significant correlation between CRSwNP recurrence and high blood eosinophil count, which may be due to differences in nasal polyp phenotypes.[12,16]

A recent study indicated that the total IgE levels in AERD patients were above 100 u/ml. However, no atopy was found in those patients.[26] The current research shows that AERD and recurrent CRSwNP have IgE levels above 100 u/mL compared to other patients. Recent studies demonstrated that higher levels of IgE in CRSwNP and AERD patients were associated with faster regrowth of nasal polyposis and also can be a cause of recurrence in CRSwNP patients.[27] Elevated levels of IgE in patients with CRSwNP highlight the potential role of IgE measurement in blood as a predictive tool for recurrence and polyp regrowth in this patient group. The presence of high IgE levels in these patients suggests a heightened allergic or inflammatory response. Elevated IgE levels in the recurrent CRSwNP groups and AERD group highlight the prediction role of this immunoglobulin.

Patients diagnosed with AERD had undergone twice as many sinus surgeries compared to those without AERD. However, in our study, patients with AERD did not experience more surgeries than those with non-AERD.[19] This difference can be a result of the genetic or demographic characteristics of the patients, which can vary among different populations or races.

Limited studies have investigated the role of SPT in determining the underlying sensitization in AERD and CRSwNP patients. The current research shows that weed pollen is the most common positive skin prick test. Also, this study suggests that patients with non-recurrent CRSwNP have a higher positive skin prick test result compared to recurrent CRSwNP. It is essential to note that in atopic patients with nasal polyposis, a negative SPT does not necessarily rule out the presence of allergies. Therefore, additional tests are required before diagnosing patients who exhibit negative SPT results for common allergens. It is essential to conduct further tests to determine the allergic status of these patients accurately.[28] On the other hand, in another study, a positive skin prick test was associated with AERD and eosinophilic polyps and with a higher percentage of positive SPT in the AERD group compared to the non-AERD group.[14] Prevalence of AERD is influenced by a family history of hypersensitivity to aspirin, a history of rhinosinusitis, and the presence of nasal polyps. Understanding these relationships can contribute to the improved identification and management of AERD in clinical practice.[29]

This study compares two subtypes of CRSwNP in different aspects such as asthma, asthma severity, AERD, skin prick test, IgE level, and eosinophil count. Few studies have evaluated the use of IgE measurement in predicting polyp recurrence. This study compares IgE levels in different groups and can be helpful in assessing the potential risk factors for the recurrence of nasal polyps. Also, this study confirms the role of AERD and asthma in the recurrence of polyps. Limited studies evaluated the role of the skin prick test. The current study discussed the potential roles of SPT in knowing underlying allergies. The study is limited due to a lack of resources for evaluating other aspects of the underlying allergies, such as interleukin measurement in the serum and tissue and eosinophils in tissue. Also, we did not have complete information on patients with previous surgeries, so we were unable to enroll the extension of the previous surgery (type of surgery) or the score of nasal polyposis in the CT scan.

In conclusion, patients with recurrent CRSwNP and AERD exhibit higher IgE levels compared to non-recurrent groups. Asthma prevalence is elevated in both AERD and recurrent CRSwNP patients. Moreover, asthma severity showed a direct correlation with both CRSwNP recurrence and AERD. Interestingly, a positive skin prick test result is more commonly observed in non-recurrent CRSwNP patients.

STATEMENT OF ETHICS

All of the patients had informed consent, and the ethics committee of the Shiraz University of Medical

Sciences approved this study. (IR. SUMS. MED.REC.1401.184).

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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