



# Inflammatory mediators in nasal secretion in patients with bronchial asthma and allergic rhinitis with or without polyposis and hypertrophic sinonasal mucosa

Svetlana Viktorovna Krasilnikova<sup>1\*</sup> , Ekaterina Ivanovna Krestova<sup>1</sup> , Tatyana Ivanovna Eliseeva<sup>1</sup> , Regina Niyazovna Khramova<sup>1,2</sup> , Ksenia Viktorovna Gorbunova<sup>1</sup> , Elena Alekseevna Leontieva<sup>1</sup> , Dmitry Yuryevich Ovsyannikov<sup>3</sup> , Natalia Anatolievna Geppe<sup>4</sup> , Nailya Iskhakovna Kubysheva<sup>5</sup> 

<sup>1</sup>Department of Hospital Pediatrics, Federal State Budgetary Educational Institution of Higher Medical Education “Privolzhsky Research Medical University” of the Ministry of Health of the Russian Federation, 603950 Nizhny Novgorod, Russian Federation

<sup>2</sup>Institute of Clinical Medicine, Lobachevsky State University of Nizhny Novgorod, 603950 Nizhny Novgorod, Russian Federation

<sup>3</sup>Medical Institute, Peoples’ Friendship University of Russia (RUDN), 117198 Moscow, Russian Federation

<sup>4</sup>Clinical Institute of Children’s Health named after N.F. Filatov, First Moscow State Medical University named after I.M. Sechenov. (Sechenov University), 119991 Moscow, Russian Federation

<sup>5</sup>Neurocognitive Research Laboratory, Kazan Federal University, 420000 Kazan, Russian Federation

**\*Correspondence:** Svetlana Viktorovna Krasilnikova, Department of Hospital Pediatrics, Federal State Budgetary Educational Institution of Higher Medical Education “Privolzhsky Research Medical University” of the Ministry of Health of the Russian Federation, 603950 Nizhny Novgorod, Russian Federation. [mashkovasv@mail.ru](mailto:mashkovasv@mail.ru)

**Academic Editor:** Irfan Rahman, University of Rochester Medical Center, USA

**Received:** January 30, 2025 **Accepted:** March 24, 2025 **Published:** April 17, 2025

**Cite this article:** Krasilnikova SV, Krestova EI, Eliseeva TI, Khramova RN, Gorbunova KV, Leontieva EA, et al. Inflammatory mediators in nasal secretion in patients with bronchial asthma and allergic rhinitis with or without polyposis and hypertrophic sinonasal mucosa. *Explor Med.* 2025;6:1001306. <https://doi.org/10.37349/emed.2025.1001306>

## Abstract

**Aim:** The pathogenetic mechanisms and predictors of the development of polyposis and hypertrophy of the sinonasal mucosa (SM) in patients with chronic allergic airway inflammation have not been clearly established. The concentration of inflammatory biomarkers in nasal secretions was determined in children and adolescents with a combined course of bronchial asthma (BA) and allergic rhinitis (AR) in the absence or presence of polyposis and hypertrophy of the SM.

**Methods:** A single-centre observational cross-sectional pilot study was conducted. 93 patients with BA aged 8 to 17 years were studied. Total Nasal Symptom Score (TNSS), sinonasal symptoms (SNOT-22), and peak nasal inspiratory flow (PNIF) were assessed. Concentrations of eosinophil cationic protein (ECP), interleukin 4 (IL-4), IL-1, total immunoglobulin E (IgE), and vascular endothelial growth factor (VEGF) in nasal secretions were determined.

**Results:** The levels of ECP, IL-4, and IL-1 in nasal secretions were statistically significantly higher in patients with the presence of polyposis and hypertrophic SM than in those without, amounting to 83.1 [31.4; 166.8] ng/mL for ECP vs. 29.5 [5.3; 49.9] ng/mL,  $P < 0.001$ , for IL-4 174.6 [68.6; 325.5] pg/mL vs. 79.5 [42.8; 146.01] pg/mL,  $P = 0.004$ , for IL-1 98.7 [33.7; 267.5] pg/mL and 48.8 [9.01; 108.2] pg/mL,  $P = 0.025$ . There were no statistically significant differences in IgE and VEGF levels in nasal secretions, all  $P >$

© The Author(s) 2025. This is an Open Access article licensed under a Creative Commons Attribution 4.0 International License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, sharing, adaptation, distribution and reproduction in any medium or format, for any purpose, even commercially, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.



0.05. Parameters such as ECP, IL-4, and IL-1 were found to be significant predictors of polyposis and hypertrophy in the formation of SM.

**Conclusions:** In patients with a combined course of BA and AR, the presence of polyposis and hypertrophy of SM is associated with higher levels of ECP, IL-4, and IL-1 in nasal secretion. This may indicate that pathological remodelling of SM is associated with both the intensity of allergic inflammation and its relationship with local activation of innate immunity.

## Keywords

Bronchial asthma, allergic rhinitis, children, adolescents, polyps, biomarkers

---

## Introduction

It is well known that the respiratory tract, from the nasal passages to the terminal bronchi, is a single functional anatomical unit [1]. In allergic diseases of the airways, both the upper airways (UA) and lower airways are involved in the process of allergic inflammation in most patients. This explains the comorbid course of bronchial asthma (BA) and allergic rhinitis/allergic rhinosinusitis (AR/ARS) [2–5]. The course of AR in a significant proportion of these patients can be accompanied by pathological remodelling of the sinonasal mucosa (SM) and the development of chronic rhinosinusitis (CRS) with or without polyps, which reduces both the patient's quality of life and the level of control of BA [6–9]. In this regard, recent consensus documents recommend mandatory assessment of UA in patients with asthma at every stage of therapy [5, 10, 11].

There is a view that CRS with polyps is the province of people over the age of 40 [12]. However, our own studies and literature data suggest that the onset of polyposis and hypertrophic SM can be observed in childhood and adolescence [8, 13, 14].

So far, it is not known exactly why the course of allergic inflammation in UA is accompanied by the formation of polyposis and hypertrophic SM in some patients [12, 15, 16]. In this regard, considerable attention has been paid to the study of the different endotypes of inflammation that form the pathogenetic basis of BA and AR, as well as their intensity and the characteristics of the reparative processes. It has been suggested that the characteristics of the inflammation and its severity may be important in the pathogenesis of the formation of pathological remodelling of the SM in these patients [12, 15, 17, 18]. Furthermore, according to Meng et al. [19], remodelling is likely to be initiated and progress in parallel with inflammation, rather than a consequence of it.

In children and adolescents with comorbid BA and AR, the predominant endotypic variant is T2-dependent inflammation. Interleukin 4 (IL-4), immunoglobulin E (IgE), and eosinophil cationic protein (ECP) are important biomarkers that characterise the T2-dependent inflammatory process [20–26]. At the same time, there are no comprehensive data on the expression of local T2 markers in patients with and without polyposis and hypertrophy SM. It should also be noted that in recent years there has been increasing information on the combination of T2 inflammation with “classical” inflammation induced by activation of innate immunity and associated with IL-1 [27–29] in patients with polyposis and SM hypertrophy. It is also important to study the role of inducers of angiogenesis and remodelling of the SM, including vascular endothelial growth factor (VEGF), which may play an important role in both polyp formation and the induction of severe tissue edema [30, 31].

Therefore, the heterogeneity of the inflammatory mechanisms involved in the development of CRS in patients with BA and AR dictates the need to search for a spectrum of biomarkers reflecting different aspects of the pathogenesis of this pathology, which is reflected in a number of recent studies [20, 21, 32–35]. However, most of the available work focuses on the study of the already-formed polyposis process using invasive histopathological techniques, mainly in the context of surgical treatment. In this regard, studies using nasal secretions are of particular interest due to the non-invasiveness of these methods, which are carried out at the stages of the debut of pathological remodelling of SM, in childhood and adolescence.

Therefore, the study of inflammatory biomarkers in nasal secretions in children and adolescents with a combined course of BA and AR and with the formation of polyposis and hypertrophy SM is relevant. It may allow clarifying the immunogenesis of these SM alterations in this category of patients for the purpose of their timely diagnosis, treatment, and prevention. Effective endotyping of patients with polyposis may be useful in the selection of targeted therapy, as suggested by international recommendations [36, 37].

### Study objective

To determine the levels of inflammatory biomarkers in nasal secretions in children and adolescents with BA and AR with and without polyposis and hypertrophic changes of the SM.

## Materials and methods

### Study design

A single-center, observational, cross-sectional study was conducted. Conditions of the study fulfillment: the study was conducted at the Children's City Clinical Hospital No. 1 in Nizhny Novgorod, Russia, from 2021 to 2024.

### Study participants

Patients with atopic BA between the ages of 8 and 17 years who were being treated for this disease participated in the study. Family history of atopy (asthma, AR, conjunctivitis, atopic dermatitis, urticaria) was assessed. Sensitisation to major aeroallergens (house dust mite, cat, dog, pollen allergens) was assessed by in vivo (prick test) or in vitro (with the determination of specific IgE) methods.

### Inclusion criteria

- (1) Diagnosis of BA established according to current international consensus documents (GINA, 2016–2021).
- (2) The age of patients is from 8 to 17 years.

### Exclusion criteria

- (1) Presence of acute infectious diseases and fever.
- (2) Presence of diabetes mellitus, autoimmune diseases, primary immunodeficiencies, cancer, atopic dermatitis, parasitic diseases, epilepsy.
- (3) Severe BA.
- (4) Systemic use of glucocorticoids and non-steroidal anti-inflammatory medications at least one month prior to the study.

### Ethical review

The study was approved by the Ethical Committee of the Volga Region Research Medical University (protocol No13, dated 10.10.2016). All participants and all primary caregivers gave written informed consent.

### Data source

#### Anthropometric indices

Basic anthropometric parameters were assessed in all patients. Anthropometric parameters [height, body weight, and body mass index (BMI)] were estimated using tables developed by the WHO, taking into account the sex and age of the patients (<https://www.who.int/tools/child-growth-standards>).

#### Spirometry

Spirometric studies were performed using MasterScreen pneumospirometer (Jaeger, Germany). The z-criterion of forced expiratory volume in 1 s/forced vital capacity (FEV<sub>1</sub>/FVC) was used to diagnose

obstructive disorders, with z-criterion values  $< -1.645$  [11]. In addition, zFVC, zFEV<sub>1</sub>, and zFEV<sub>1</sub>/FVC were calculated using the Global Lung Function Initiative calculator (<http://gli-calculator.ersnet.org/index.html>) developed with the support of the European Respiratory Society (ERS, <https://www.ersnet.org>).

All patients underwent an otorhinolaryngological examination: routine otorhinolaryngological examination, endoscopic examination and computed tomography of the sinuses, peak nasal inspiratory (PNIF) flow measurement, quantitative assessment of sinonasal symptoms using the Sino-Nasal Outcome Test-22 (SNOT-22) [28] and the Total Nasal Symptom Score (TNSS) [29].

### Determination of inflammatory mediators

The collection of nasal secretion for the subsequent determination of the concentration of ECP, IL-4, IgE, IL-1, and VEGF was performed using sponge strips “Merozel” manufactured by Medtronic (USA). Sponge strips of predetermined mass were placed under the middle nasal cavity of each half of the nose for 2 min. The strips with absorbed nasal secretion were then reweighed, the mass of secretion obtained was determined, and 1.5 mL of physiological solution was added to the tube containing the sponge strips. The tube was placed on a shaker for 10 min and centrifuged at 1,500 rpm for 10 min. The selected supernatant was stored at  $-20^{\circ}\text{C}$  for a maximum of two weeks. The concentration of IL-1 $\beta$ , IL-4, and IgE in nasal secretion was determined by enzyme-linked immunosorbent assay on an automated analyser ALISEI Quality System (Italy) using Vector Best test systems (Russia) and ECP using Aviscera Bioscience kit (USA). Patients did not receive any topical endonasal medication for at least 24 h prior to the study.

### Nasal airflow

This was assessed noninvasively by measuring the PNIF (L/min) during forced inspiration using a portable PNIF meter (Incheck DIAL, Clement Clarke International, Harlow, UK). The mean value of 3 satisfactory maximal nasal inspirations was calculated.

### Statistical analysis

The study was a pilot study and no sample size was calculated. Analyses were performed using Statgraphics Centurion v.16 (Statgraphics Technologies, Inc., The Plains, Virginia, USA). Quantitative measures were assessed for conformity to a normal distribution. Data are presented as Me [Q1; Q3], where Me is the median, [Q1; Q3] are the 1st and 3rd quartiles due to a distribution other than normal. The Mann-Whitney test was used to compare quantitative variables in two independent groups. Correlation analysis was performed using Spearman’s correlation coefficient. Differences were considered statistically significant at  $P < 0.05$ . The sensitivity and specificity of changes in the studied parameters were evaluated by linear regression method with receiver operator characteristic (ROC) curves construction.

## Results

A total of 93 patients aged 8–17 years were studied, of whom 71% (66/93) were boys. The median age of the examined patients was 13.0 [10.0; 16.0] years, whereby patients with polyposis and hypertrophy SM were statistically significantly older,  $P < 0.001$  (Table 1). Patients in the compared groups did not show statistical differences in z-height,  $P = 0.258$ , and zFEV<sub>1</sub>/FVC,  $P = 0.385$ . The zBMI values were statistically significantly lower in the group of patients with polyposis and hypertrophy SM,  $P = 0.023$ , and the same patients showed statistically significantly lower zFVC and zFEV<sub>1</sub> values,  $P = 0.008$  and  $P = 0.007$ , respectively.

As expected, patients with SM hypertrophy were characterised by statistically significantly lower nasal respiratory function scores,  $P = 0.047$ , and had statistically significantly higher TNSS and SNOT-22 scores,  $P = 0.012$  and  $P = 0.001$ , respectively.

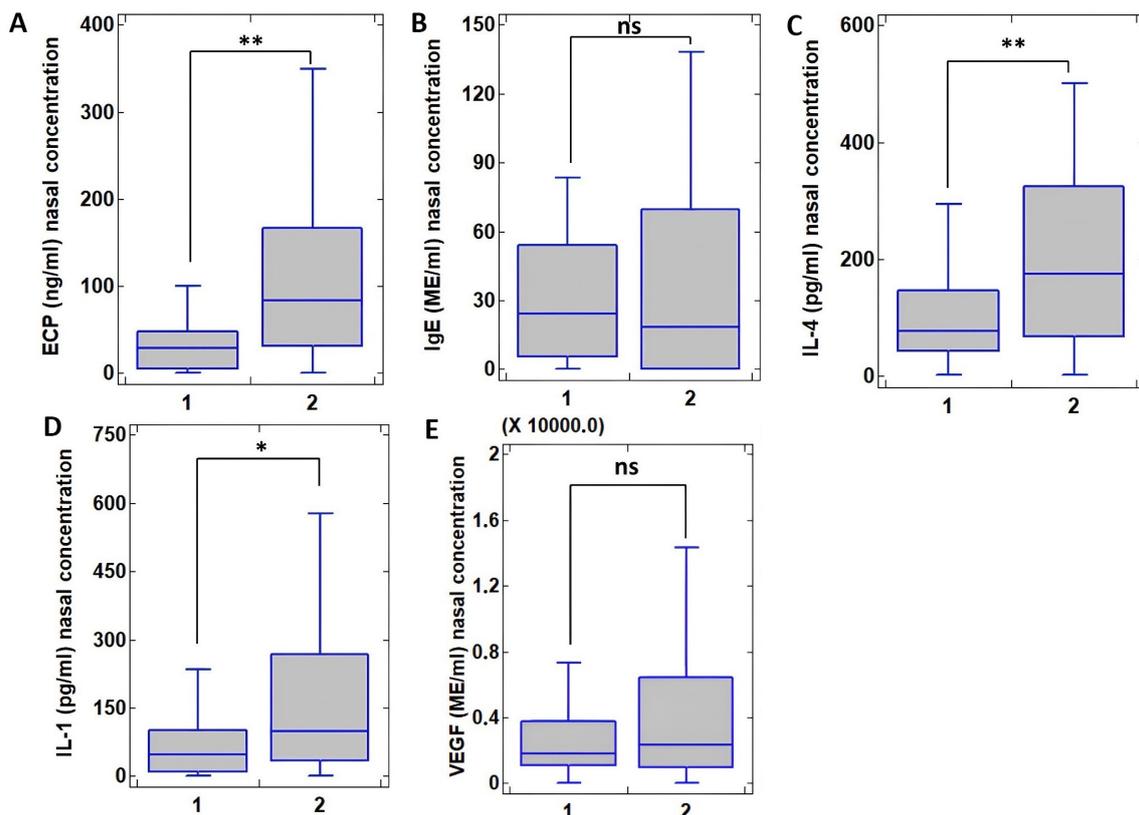
The levels of ECP, IL-4, and IL-1 in nasal secretion were considered statistically significantly higher in patients with the presence of polyposis and hypertrophy SM than in those without, amounting to ECP 83.1 [31.4; 166.8] ng/mL vs. 29.5 [5.3; 49.9] ng/mL,  $P < 0.001$ ; for IL-4 174.6 [68.6; 325.5] pg/mL, vs. 79.5 [42.8; 146.01] pg/mL,  $P = 0.004$ ; for IL-1 98.7 [33.7; 267.5] pg/mL and 48.8 [9.01; 108.2] pg/mL,  $P = 0.025$

**Table 1. Clinical characteristics of patients**

Data	All patients	Without polyposis and hypertrophy SM	With polyposis and hypertrophy SM	P-value
Patients, N (%)	93 (100%)	50 (53.8%)	43 (46.2%)	0.382
Age	13.0 [10.0; 16.0]	11.0 [9.0; 13.0]	16.0 [14.0; 17.0]	< 0.001
z-height	0.59 [-0.19; 1.68]	0.59 [0.03; 1.86]	0.56 [-0.26; 1.05]	0.258
zBMI	-0.03 [-0.81; 1.15]	-0.01 [-0.46; 1.3]	-0.54 [-1.1; 0.31]	0.023
zFVC	1.2 [0.4; 2.0]	1.4 [0.7; 2.2]	0.6 [-0.3; 1.9]	0.008
zFEV <sub>1</sub> /FVC	-1.3 [-2.1; -0.6]	-1.4 [-2.1; -0.8]	-1.2 [-2.3; -0.04]	0.385
zFEV <sub>1</sub>	0.2 [-0.9; 1.01]	0.5 [-0.5; 1.1]	-0.5 [-1.4; 0.4]	0.007
RPF (L/min)	40.0 [30.2; 49.8]	41.7 [33.3; 56.0]	38.3 [28.0; 45.7]	0.047
TNSS (points)	6.0 [4.0; 8.0]	5.0 [3.5; 7.5]	8.0 [5.0; 8.0]	0.012
SNOT-22 (points)	18.0 [12.0; 25.0]	16.0 [10.0; 21.0]	22.0 [15.0; 31.0]	0.001
Eosinophils (10 <sup>9</sup> /L)	0.3 [0.2; 0.6]	0.4 [0.2; 0.7]	0.3 [0.1; 0.5]	0.378
Total IgE (ME/mL)	183.3 [80.2; 399.7]	178.4 [92.6; 378.8]	201.6 [80.2; 399.7]	0.811

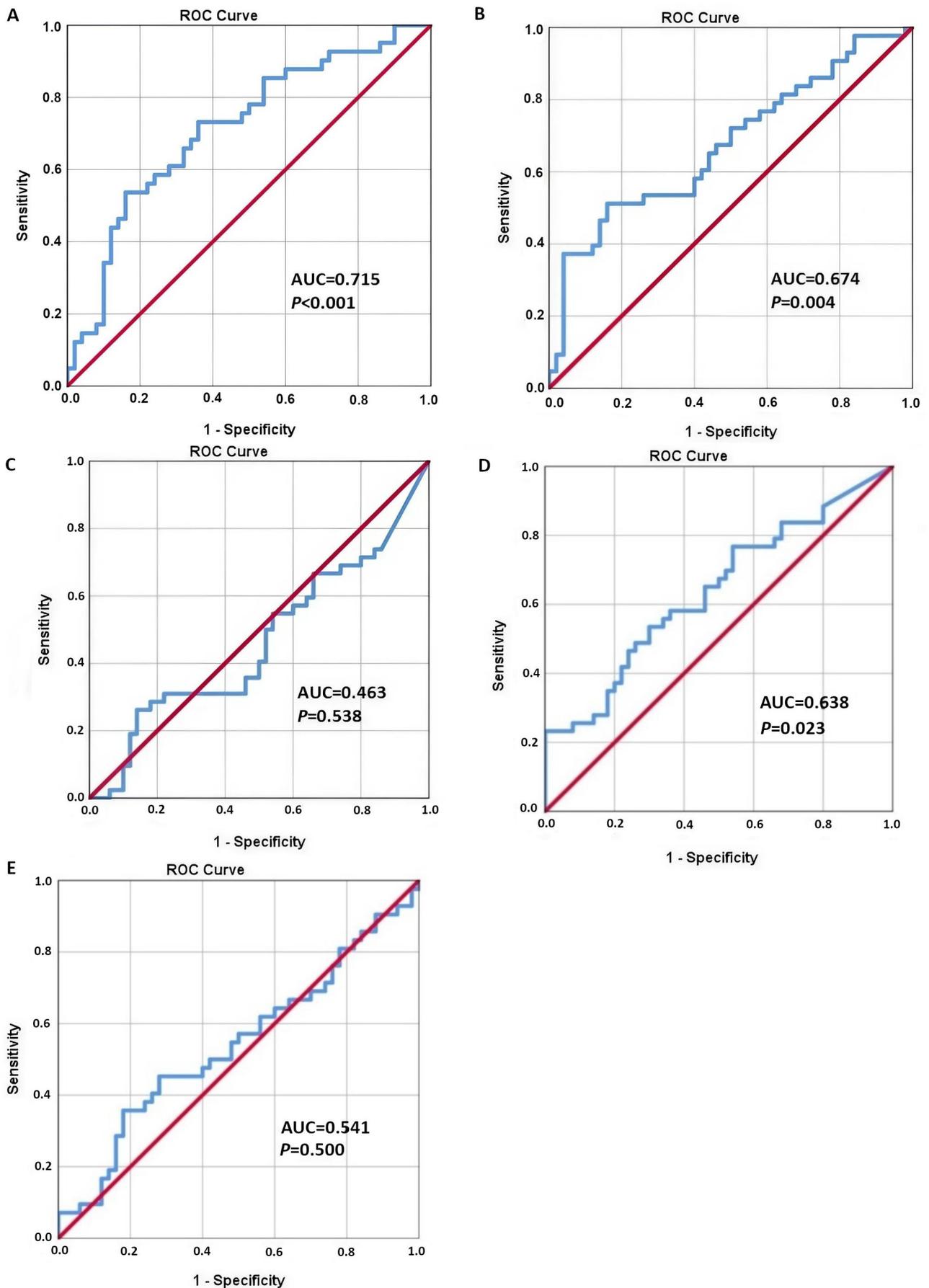
Data are presented as Me [Q1; Q3], where Me is the median, [Q1; Q3] are the 1st and 3rd quartiles due to a distribution other than normal. SNOT-22: Sino-Nasal Outcome Test-22; SM: sinonasal mucosa; BMI: body mass index; FEV<sub>1</sub>/FVC: forced expiratory volume in 1 s/forced vital capacity; RPF: renal plasma flow; TNSS: Total Nasal Symptom Score

(Figure 1). Concentrations of both IgE and VEGF were comparable in the absence and presence of hypertrophy SM, with IgE 26.1 [5.6; 54.2] ME/mL and 16.8 [0; 62.9] ME/mL,  $P = 0.444$ , for VEGF 1,871.6 [1,102.6; 3,790.8] ME/mL and 2,624.2 [956.9; 6,448.57] ME/mL,  $P = 0.429$ .



**Figure 1. Concentration of cytokines in nasal secretion in patients with bronchial asthma and allergic rhinitis without polyposis/hypertrophic sinonasal mucosal changes (1, N = 50) and with polyposis/hypertrophic sinonasal mucosal changes (2, N = 43) evaluated by paired Wilcoxon test. (A) Concentration of eosinophil cationic protein (ECP), ng/mL; (B) Concentration of immunoglobulin E (IgE), ME/mL; (C) Concentration of interleukin 4 (IL-4), pg/mL; (D) Concentration of IL-1, pg/mL; (E) Concentration of vascular endothelial growth factor (VEGF), ME/mL. Values at  $P < 0.05$  were considered statistically significant and are shown as \* ( $P < 0.05$ ) and \*\* ( $P < 0.01$ ), ns: not significant ( $P > 0.05$ )**

ROC curves were used to assess the predictive potential of the nasal secretion biomarkers studied for the development of polyposis and hypertrophy SM in children and adolescents with BA and AR (Figure 2).



**Figure 2. ROC curves of the analysis of prognostic factors for polyposis and hypertrophy of the sinonasal mucosa in children and adolescents with asthma and allergic rhinitis. (A)** Concentration of eosinophil cationic protein (ECP), ng/mL; **(B)** Concentration of interleukin 4 (IL-4), pg/mL; **(C)** Concentration of immunoglobulin E (IgE), ME/mL; **(D)** Concentration of IL-1, pg/mL; **(E)** Concentration of vascular endothelial growth factor (VEGF), ME/mL. ROC: receiver operator characteristic; AUC: area under the curve

The concentration of ECP in nasal secretion showed good prognostic value (AUC = 0.715) (Table 2). The ROC curve of IL-4 and IL-1 levels showed an influence of these cytokines on the formation of polyposis and hypertrophy SM (AUC was 0.674 and 0.638, respectively). While the ROC curve of IgE level did not show the significance of this cytokine in predicting the development of sinonasal hypertrophy (AUC = 0.463). The ROC analysis also showed no significant effect of VEGF levels on the development of polyposis and hypertrophic SM in the study cohort (AUC = 0.541).

**Table 2. Regression analysis of prognostic factors for polyposis and hypertrophic changes of sinonasal mucosa in children and adolescents with asthma and allergic rhinitis**

Data	AUC	95% CI	Sensitivity (%)	Specificity (%)	OR [95% CI]	P-value
ECP	0.715	0.715 ± 0.055	78.0	48.0	1.008 [1.002–1.013]	< 0.001
IL-4	0.674	0.674 ± 0.057	74.4	46.0	1.005 [1.001–1.008]	0.004
IL-1	0.638	0.638 ± 0.058	76.7	46.0	1.003 [1.000–1.006]	0.023
VEGF	0.541	0.541 ± 0.062	71.4	24.0	0.840 [0.332–0.939]	0.500
IgE	0.463	0.463 ± 0.062	69.0	22.0	0.694 [0.193–0.840]	0.538

AUC: area under the curve; OR: odds ratio; ECP: eosinophil cationic protein; IL-4: interleukin 4; IgE: immunoglobulin E; VEGF: vascular endothelial growth factor

## Discussion

The present study investigated the concentration of ECP, IL-4, total IgE, IL-1, and VEGF in nasal secretion in children and adolescents with a combined course of BA and AR/ARS, taking into account the absence or presence of polyposis and hypertrophy SM. To our knowledge, this is the first such study in children and adolescents with BA.

Patients with polyposis and SM hypertrophy were statistically significantly older ( $P < 0.001$ ) and, as expected, had lower nasal respiratory function scores ( $P = 0.047$ ) and higher nasal (TNSS) and sinonasal (SNOT-22) complaints ( $P = 0.012$  and  $P = 0.001$ , respectively).

According to the results of our study, the level of ECP, IL-4, and IL-1 in nasal secretion was statistically significantly higher in patients with the presence of polyposis and hypertrophy SM than in patients with their absence. This may indicate that in children and adolescents with the combined course of BA and AR, the formation of polyposis and SM hypertrophy is associated with greater expression of both T2-dependent inflammatory processes (higher levels of ECP and IL-4) and primary immune response (higher IL-1 concentration).

In the literature available to us, we found no studies devoted to analysing the concentration of inflammatory biomarkers in nasal secretions in children and adolescents with a combined course of BA and AR/ARS, taking into account the presence or absence of polyposis SM. Nevertheless, our data are generally consistent with the results of studies in adult patients with formed polyps who have undergone surgical treatment, in which an increase in biomarkers reflecting the expression of different inflammatory endotypes has been demonstrated [32, 38–41]. For example, Perić et al. [32] found higher levels of ECP not only in nasal polyp tissue but also in nasal secretions in adult patients with atopy. At the same time, according to Turner et al. [42], IL-5 and IL-13 levels in nasal mucus were elevated in subjects with CRS compared to controls, whereas no significant difference was observed for IL-4. The data we have obtained generally support the view that inflammation of the T2-endotype is of fundamental importance in the formation of the polyposis process in patients with a combined course of BA and AR, which, in addition to the increase in IL-4 production and ECP concentration that we have shown, is accompanied by an increase in the production of IL-5 and IL-13, which were not studied in this work. Stimulation of Th2 cells, type 2 innate lymphoid cells, epithelial cell injury, *Staphylococcus aureus* enterotoxins and autoimmune antibodies play an important role in enhancing T2 inflammation and the formation of CRS with polyps [43].

The efficacy of modern therapies in the treatment of nasal polyposis using genetically engineered immunobiological drugs (GIIBPs) targeting components of the T2-dependent immune response, including IL-4 and eosinophil infiltration, can also be considered as an indirect agreement with our results [44, 45]. In

our work, we found increased IL-1 levels in patients with polyposis and hypertrophic CM. These results again emphasise that CRS with polyps in children and adolescents with BA and AR is a multifactorial and heterogeneous pathological process that may be associated with the activation of innate immunity [46, 47]. Our data on the potential involvement of IL-1 in the pathogenesis of polyposis CRS formation in patients with the combined course of BA and AR are consistent with the studies [29, 48].

Although total IgE is considered an important biomarker of Th2-dependent immune responses, we found no differences in its levels in nasal secretions between patients with and without polyposis and hypertrophic SM, in contrast to, for example, ECP levels. This may be due to the fact that ECP can be considered as an integral biomarker of eosinophilic inflammation, which, in turn, can be initiated without the involvement of IgE, through the initiation of CCL-2 cells [49]. Our findings are in partial agreement with the results of Vlaykov et al. [50], who found no differences in the concentration of IgE in nasal lavage between healthy subjects and patients with AR ( $P = 0.312$ ), whereas IL-4 was statistically higher in patients with AR.

We also found no differences in VEGF levels in nasal secretions between patients with and without polyposis and hypertrophy SM,  $P = 0.429$ . This is in contrast to previous studies of increased concentration of this protein in polyp tissue [30, 51]. However, we were unable to find studies on VEGF levels in nasal secretion in children and adolescents with BA and nasal polyps.

Therefore, our findings are consistent with the view that CRS with polyps is a multifactorial and heterogeneous inflammatory disease of SM, including patients with a predominance of T2-dependent mechanisms [12, 15, 52]. The inflammatory pattern of SM in patients with combined BA and AR with hypertrophic and polyposis SM is associated not only with increased expression of the T2 inflammatory cytokines ECP and IL4, but also with activation of the primary immunity, which is probably evidenced by elevated IL-1 levels. Understanding the immunogenesis of polyposis SM is important for selecting the most effective therapies. Without this knowledge, it is difficult to develop personalised treatment approaches based on individual patient characteristics.

Limitations of this study were: no control group of healthy participants to compare the results, no stratification of the sample by age groups, sex, and puberty, the relationship between clinical and functional parameters and biomarkers was not analysed.

## Abbreviations

AR: allergic rhinitis

BA: bronchial asthma

BMI: body mass index

CRS: chronic rhinosinusitis

ECP: eosinophil cationic protein

FEV<sub>1</sub>/FVC: forced expiratory volume in 1 s/forced vital capacity

IgE: immunoglobulin E

IL-4: interleukin 4

ROC: receiver operator characteristic

SM: sinonasal mucosa

SNOT-22: Sino-Nasal Outcome Test-22

TNSS: Total Nasal Symptom Score

UA: upper airways

VEGF: vascular endothelial growth factor

## Declarations

### Author contributions

SVK: Conceptualization, Resources, Investigation, Methodology, Validation, Visualization, Writing—original draft, Writing—review & editing. TIE: Conceptualization, Investigation, Formal analysis, Supervision, Resources, Writing—original draft, Writing—review & editing. EIK and EAL: Resources, Investigation, Methodology. RNK: Data curation, Software. KVG: Resources, Data curation. DYO, NAG, and NIK: Writing—review & editing. All authors read and approved the final manuscript.

### Conflicts of interest

The authors declare no competing interests.

### Ethical approval

The study was approved by the Ethical Committee of the Volga Region Research Medical University (protocol No13, dated 10.10.2016).

### Consent to participate

All participants and all primary caregivers gave written informed consent.

### Consent to publication

Not applicable.

### Availability of data and materials

The data used to support the findings of this study are available from the corresponding author (Svetlana Viktorovna Krasilnikova, [mashkovasv@mail.ru](mailto:mashkovasv@mail.ru)) upon request.

### Funding

Not applicable.

### Copyright

© The Author(s) 2025.

## Publisher's note

Open Exploration maintains a neutral stance on jurisdictional claims in published institutional affiliations and maps. All opinions expressed in this article are the personal views of the author(s) and do not represent the stance of the editorial team or the publisher.

## References

1. Vizuete JAC, Sastre J, Bernal ADC, Picado C, Moragón EM, García JMI, et al. Asthma, rhinitis, and nasal polyp multimorbidities. *Arch Bronconeumol (Engl Ed)*. 2019;55:146–55. [DOI] [PubMed]
2. Global Strategy for Asthma Management and Prevention (2019 update) [Internet]. Global Initiative for Asthma; © 2019 [cited 2024 Dec 4]. Available from: <https://ginasthma.org/wp-content/uploads/2019/06/GINA-2019-main-report-June-2019-wms.pdf>
3. Hossny E, Adachi Y, Anastasiou E, Badellino H, Custovic A, El-Owaidy R, et al. Pediatric asthma comorbidities: Global impact and unmet needs. *World Allergy Organ J*. 2024;17:100909. [DOI] [PubMed] [PMC]
4. Reddel HK, FitzGerald JM, Bateman ED, Bacharier LB, Becker A, Brusselle G, et al. GINA 2019: a fundamental change in asthma management: Treatment of asthma with short-acting bronchodilators alone is no longer recommended for adults and adolescents. *Eur Respir J*. 2019;53:1901046. [DOI] [PubMed]

5. Brożek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines-2016 revision. *J Allergy Clin Immunol*. 2017;140:950–8. [DOI] [PubMed]
6. Eliseeva TI, Krasilnikova SV, Geppe NA, Babaev SY, Tush EV, Khaletskaia OV, et al. Effect of Nasal Obstructive Disorders on Sinonasal Symptoms in Children with Different Levels of Bronchial Asthma Control. *Can Respir J*. 2018;2018:4835823. [DOI] [PubMed] [PMC]
7. Canonica GW, Malvezzi L, Blasi F, Paggiaro P, Mantero M, Senna G, et al. Chronic rhinosinusitis with nasal polyps impact in severe asthma patients: Evidences from the Severe Asthma Network Italy (SANI) registry. *Respir Med*. 2020;166:105947. [DOI] [PubMed]
8. Eruslankin NI, Vagina AA, Krasilnikova SV, Khramov AA, Bulgakova VA, Balabolkin II, et al. Hypertrophic and polypous changes in the sinonasal mucosa in children with atopic bronchial asthma and allergic rhinitis. *Allergology and Immunology in Pediatrics*. 2021;1:35–43. [DOI]
9. Castillo JA, Plaza V, Rodrigo G, Juliá B, Picado C, Fernández C, et al. Chronic rhinosinusitis with nasal polyps and allergic rhinitis as different multimorbid treatable traits in asthma. *J Allergy Clin Immunol Glob*. 2023;2:100134. [DOI] [PubMed] [PMC]
10. Foxman EF, Storer JA, Fitzgerald ME, Wasik BR, Hou L, Zhao H, et al. Temperature-dependent innate defense against the common cold virus limits viral replication at warm temperature in mouse airway cells. *Proc Natl Acad Sci U S A*. 2015;112:827–32. [DOI] [PubMed] [PMC]
11. Wise SK, Damask C, Roland LT, Ebert C, Levy JM, Lin S, et al. International consensus statement on allergy and rhinology: Allergic rhinitis - 2023. *Int Forum Allergy Rhinol*. 2023;13:293–859. [DOI] [PubMed]
12. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. *Rhinology*. 2020;58:1–464. [DOI] [PubMed]
13. Huang C, Chang P, Huang Y, Lee T, Huang C, Wu P. Clinical Characteristics of Eosinophilic Chronic Rhinosinusitis with Nasal Polyps in Adolescents. *J Asthma Allergy*. 2023;16:1197–206. [DOI] [PubMed] [PMC]
14. Caimmi D, Matti E, Pelizzo G, Marseglia A, Caimmi S, Labò E, et al. Nasal polyposis in children. *J Biol Regul Homeost Agents*. 2012;26:S77–83. [PubMed]
15. Kato A, Schleimer RP, Bleier BS. Mechanisms and pathogenesis of chronic rhinosinusitis. *J Allergy Clin Immunol*. 2022;149:1491–503. [DOI] [PubMed] [PMC]
16. Chen F, Wen L, Qiao L, Shi Z, Xue T, Chen X, et al. Impact of Allergy and Eosinophils on the Morbidity of Chronic Rhinosinusitis with Nasal Polyps in Northwest China. *Int Arch Allergy Immunol*. 2019;179:209–14. [DOI] [PubMed]
17. Schleimer RP. Immunopathogenesis of Chronic Rhinosinusitis and Nasal Polyposis. *Annu Rev Pathol*. 2017;12:331–57. [DOI] [PubMed] [PMC]
18. Stevens WW, Schleimer RP, Kern RC. Chronic Rhinosinusitis with Nasal Polyps. *J Allergy Clin Immunol Pract*. 2016;4:565–72. [DOI] [PubMed] [PMC]
19. Meng J, Zhou P, Liu Y, Liu F, Yi X, Liu S, et al. The development of nasal polyp disease involves early nasal mucosal inflammation and remodelling. *PLoS One*. 2013;8:e82373. [DOI] [PubMed] [PMC]
20. Perić A, Vojvodić D, Vukomanović-Đurđević B, Baletić N. Eosinophilic inflammation in allergic rhinitis and nasal polyposis. *Arh Hig Rada Toksikol*. 2011;62:341–8. [DOI] [PubMed]
21. Tomassen P, Vandeplas G, Zele TV, Cardell L, Arebro J, Olze H, et al. Inflammatory endotypes of chronic rhinosinusitis based on cluster analysis of biomarkers. *J Allergy Clin Immunol*. 2016;137:1449–56.e4. [DOI] [PubMed]
22. Cheng W, Zheng C, Tian J, Shi G. T helper cell population and eosinophilia in nasal polyps. *J Investig Allergol Clin Immunol*. 2007;17:297–301. [PubMed]
23. Kato A. Group 2 Innate Lymphoid Cells in Airway Diseases. *Chest*. 2019;156:141–9. [DOI] [PubMed] [PMC]

24. Colas L, Magnan A, Brouard S. Immunoglobulin E response in health and disease beyond allergic disorders. *Allergy*. 2022;77:1700–18. [DOI] [PubMed]
25. Krasil'nikova SV, Eliseeva TI, Tush EV, Bol'shova EV, Kubysheva NI, Balabolkin II. Features of local inflammation of nasal mucosa in children with bronchial asthma. *Russian Otorhinolaryngology*. 2020; 19:22–30. [DOI]
26. Wang M, Bu X, Luan G, Lin L, Wang Y, Jin J, et al. Distinct type 2-high inflammation associated molecular signatures of chronic rhinosinusitis with nasal polyps with comorbid asthma. *Clin Transl Allergy*. 2020;10:26. [DOI] [PubMed] [PMC]
27. Pawankar R, Hayashi M, Yamanishi S, Igarashi T. The paradigm of cytokine networks in allergic airway inflammation. *Curr Opin Allergy Clin Immunol*. 2015;15:41–8. [DOI] [PubMed]
28. Lim HF, Nair P. Airway Inflammation and Inflammatory Biomarkers. *Semin Respir Crit Care Med*. 2018;39:56–63. [DOI] [PubMed]
29. Xie X, Wang P, Jin M, Wang Y, Qi L, Wu C, et al. IL-1 $\beta$ -induced epithelial cell and fibroblast transdifferentiation promotes neutrophil recruitment in chronic rhinosinusitis with nasal polyps. *Nat Commun*. 2024;15:9101. [DOI] [PubMed] [PMC]
30. Hu K, Lee F, Cheng Y, Huang H. Vascular endothelial growth factor and children featuring nasal polyps. *Int J Pediatr Otorhinolaryngol*. 2007;71:23–8. [DOI] [PubMed]
31. Nemati S, Keihanian F, Saeidinia A, Bakhshaei M. Effect Of Bevacizumab On Growth Of Human Nasal Polyposis In Vitro; An Off-Label Use Of Anti-Angiogenic Agent For Nasal Polyposis Treatment. *Drug Des Devel Ther*. 2019;13:3383–9. [DOI] [PubMed] [PMC]
32. Perić A, Vojvodić D, Radulović V, Vukomanović-Đurđević B, Miljanović O. Correlation between cytokine levels in nasal fluid and eosinophil counts in nasal polyp tissue in asthmatic and non-asthmatic patients. *Allergol Immunopathol (Madr)*. 2011;39:133–9. [DOI] [PubMed]
33. Krasilnikova SV, Tush EV, Frolov PA, Ovsyannikov DY, Terentyeva AB, Kubysheva NI, et al. Periostin as a Biomarker of Allergic Inflammation in Atopic Bronchial Asthma and Allergic Rhinitis (a Pilot Study). *Sovrem Tekhnologii Med*. 2021;12:37–45. [DOI] [PubMed] [PMC]
34. Krasilnikova SV, Ovsyannikov DY, Eliseeva TI, Tush EV, Bolshova EV, Larin RA, et al. Thymic Stromal Lymphopoietin as a Predictor of Hypertrophic Changes in the Nasal Mucosa in Children with Atopic Bronchial Asthma and Allergic Rhinitis. *Pediatria Journal named after GN Speransky*. 2020;99:71–8. [DOI]
35. Jiang L, Zeng Y, Huang Z, Tang Y, Zeng Q, Liu W, et al. Immunopathologic characteristics of Chinese pediatric patients with chronic rhinosinusitis. *World Allergy Organ J*. 2021;14:100616. [DOI] [PubMed] [PMC]
36. Bachert C, Han JK, Wagenmann M, Hosemann W, Lee SE, Backer V, et al. EUFOREA expert board meeting on uncontrolled severe chronic rhinosinusitis with nasal polyps (CRSwNP) and biologics: Definitions and management. *J Allergy Clin Immunol*. 2021;147:29–36. [DOI] [PubMed]
37. Corso ED, Bilò MB, Matucci A, Seccia V, Braido F, Gelardi M, et al. Personalized Management of Patients with Chronic Rhinosinusitis with Nasal Polyps in Clinical Practice: A Multidisciplinary Consensus Statement. *J Pers Med*. 2022;12:846. [DOI] [PubMed] [PMC]
38. Lorenzo GD, Drago A, Pellitteri ME, Candore G, Colombo A, Gervasi F, et al. Measurement of inflammatory mediators of mast cells and eosinophils in native nasal lavage fluid in nasal polyposis. *Int Arch Allergy Immunol*. 2001;125:164–75. [DOI] [PubMed]
39. Savlevich EL, Kurbacheva OM, Egorov VI, Dyneva ME, Shilovskiy IP, Khaitov MR. Gene expression levels of cytokines in different phenotypes of CRSwNP. *Vestn Otorinolaringol*. 2019;84:42–7. [DOI] [PubMed]
40. Sun D, Joo Y, Auo H, Kang J. Clinical significance of eosinophilic cationic protein levels in nasal secretions of patients with nasal polyposis. *Eur Arch Otorhinolaryngol*. 2009;266:981–6. [DOI] [PubMed]

41. Nabavi M, Arshi S, Bahrami A, Aryan Z, Bemanian MH, Esmaeilzadeh H, et al. Increased level of interleukin-13, but not interleukin-4 and interferon- $\gamma$  in chronic rhinosinusitis with nasal polyps. *Allergol Immunopathol (Madr)*. 2014;42:465–71. [DOI] [PubMed]
42. Turner JH, Li P, Chandra RK. Mucus T helper 2 biomarkers predict chronic rhinosinusitis disease severity and prior surgical intervention. *Int Forum Allergy Rhinol*. 2018;8:1175–83. [DOI] [PubMed] [PMC]
43. Aazami H, Seif F, Ghalehbaghi B, Mohebbi A, Ahmadi A, Babaheidarian P, et al. Levels of total IgA and IgA subclasses in the serum of chronic rhinosinusitis patients. *Med J Islam Repub Iran*. 2018;32:94. [DOI] [PubMed] [PMC]
44. Kariyawasam HH. Chronic rhinosinusitis with nasal polyps: mechanistic insights from targeting IL-4 and IL-13 via IL-4R $\alpha$  inhibition with dupilumab. *Expert Rev Clin Immunol*. 2020;16:1115–25. [DOI] [PubMed]
45. Guo C, Liu F, Wang D, Liu Z. Type 2 Biomarkers for the Indication and Response to Biologics in CRSwNP. *Curr Allergy Asthma Rep*. 2023;23:703–13. [DOI] [PubMed]
46. Hannikainen P, Kahn C, Toskala E. Allergic Rhinitis, Rhinosinusitis, and Asthma: Connections Across the Unified Airway. *Otolaryngol Clin North Am*. 2024;57:171–8. [DOI] [PubMed]
47. Ambrosino P, Marcuccio G, Raffio G, Formisano R, Candia C, Manzo F, et al. Endotyping Chronic Respiratory Diseases: T2 Inflammation in the United Airways Model. *Life (Basel)*. 2024;14:899. [DOI] [PubMed] [PMC]
48. Mohamad S, Hamid SSA, Azlina A, Shukri NM. Association of *IL-1* gene polymorphisms with chronic rhinosinusitis with and without nasal polyp. *Asia Pac Allergy*. 2019;9:e22. [DOI] [PubMed] [PMC]
49. Carsuzaa F, Bequignon E, Dufour X, de Bonnecaze G, Lecron JC, Favot L. Cytokine Signature and Involvement in Chronic Rhinosinusitis with Nasal Polyps. *Int J Mol Sci*. 2021;23:417. [DOI] [PubMed] [PMC]
50. Vlaykov A, Miśkiewicz-Orczyk K. Effect of IL-4, IL-5, IL-13, and IgE on Nasal Congestion in Patients with Allergic Rhinitis. *Open Access Macedonian Journal of Medical Sciences*. 2022;10:2225–9. [DOI]
51. Delshad AA, Nadoushan MJ, Davati A, Rostami A. Expression of Vascular Endothelial Growth Factor in Nasal Polyp and Chronic Rhinosinusitis. *Iran J Pathol*. 2016;11:231–7. [PubMed] [PMC]
52. Shah SA, Kobayashi M. Pathogenesis of chronic rhinosinusitis with nasal polyp and a prominent T2 endotype. *Heliyon*. 2023;9:e19249. [DOI] [PubMed] [PMC]