El-Anwar *et al.*
The Egyptian Journal of Otolaryngology (2022) 38:82
https://doi.org/10.1186/s43163-022-00276-0

The Egyptian Journal of Otolaryngology

ORIGINAL ARTICLE Open Access

Assessment of the blood eosinophil count in different grades of nasal polyps

Mohammad Waheed El-Anwar*, Mohamed Adel Mobasher and Ehsan Hindawy

Abstract

Background: Blood eosinophil count is significantly correlated with eosinophil infiltration in the nasal polyps; so, it could be a good marker for the nasal polyp eosinophilic inflammation.

Objective: Assessment of different peripheral eosinophil counts in different nasal polyps grading in allergic rhinitis patients.

Methods: A study was applied to 160 patients with allergic rhinitis (AR). Computed tomography (CT) was done preoperative then nasal polyps grading was assessed by nasal endoscopy. Peripheral eosinophil counts were checked in a blood sample for all patients. Then, a statistical analysis of the data was done.

Results: The study included 160 patients. Within 54 AR patients with no nasal polypi, eosinophil counts ranged between 0.001 × 10^3 µl and 0.907 × 10^3 µl with a mean of 0.2399 (SD = 0.2153). While within 106 patients with nasal polyps, eosinophil counts ranged between 0.05 × 10^3 µl and 14.7 × 10^3 µl with a mean of 1.6645 (SD = 3.06) with a significant difference ($p = 0.0008$, $t = 3.418$). The eosinophil counts were statistically significantly more in advanced grades of the nasal polyps ($p < 0.0001$, $F = 9248$).

Conclusion: Measuring peripheral eosinophil counts is simple, low cost, safe, and directly proportionate with different grades of nasal polyps. It can be used as a reliable marker to predict the severity of nasal polyps and consequently predict the prognosis of sinus disease and quality of life.

Keywords: Nasal polyps, Eosinophil, Endoscopic sinus surgery, Allergic rhinitis, Recurrence

Introduction

Chronic rhinosinusitis (CRS) is the most common chronic inflammatory disease of the upper airway [1]. CRS is divided into two types according to the absence or presence of nasal polyps (NPs): CRS without NPs (CRSsNP) and CRS with NPs (CRSwNP) [2].

CRS is divided into two phenotypes according to CT and endoscopy findings: CRSsNP and CRSwNP [3] which are characterized by the presence of nasal polyps, signs and symptoms lasting more than 8–12 weeks [4, 5]. The EPOS2020 steering group classified CRS into primary and secondary and categorized each into diffuse and localized disease depending on the anatomical distribution. Then, primary CRS was classified into type 2 or non-type 2 while localized primary CRS was then subclassified clinically into two phenotypes: isolated sinusitis or allergic fungal rhinosinusitis. For diffuse CRS, the clinical phenotypes are predominantly eCRS and non-eCRS [6]. Immunologically, NPs are divided into three types: type 1, immune response which is common in Asia [7] and characterized by neutrophilic infiltration; type 2, which is characterized mainly by eosinophilic infiltration, and this type is more common in Caucasians [8]; and type 3 immune response is characterized by a high level of the IL-17 cytokine, mixed inflammatory cell pattern, and is associated with frequent asthma exacerbations [9].

CRSwNP affects about 1–4% of the general population and 25–30% of CRS patients [6]. The etiology of NPs is

*Correspondence: mwenteg1973@gmail.com

Otorhinolaryngology, Head and Neck Surgery Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt

multifactorial: allergy and inflammatory mediators such as eosinophils which contain leukotrienes, eosinophilic cationic protein, major basic protein, platelet-activating factor, eosinophilic peroxidases, and other vasoactive substances that cause mucosal damage. These may play a critical role in the development of nasal polyps [10]. Also, there are non-allergic causes of NPs such as cystic fibrosis [1].

CRSwNP is often characterized by eosinophilic inflammation with increased levels of T helper 2 (Th2) cytokines [11, 12]. Marked eosinophilic tissue infiltration in CRSwNP is frequently associated with extensive sinus disease [11, 13], comorbid asthma, olfactory dysfunction, high recurrence rate after surgery, and less improvement in both disease-specific and general quality of life [14].

CRSwNP is frequently associated with asthma and allergic rhinitis, but the cellular and molecular mechanisms that contribute to the clinical symptoms are not fully understood.

It was found that blood eosinophil count is significantly correlated with eosinophil infiltration in the nasal polyps; the blood eosinophil count could be a good marker for the eosinophilic inflammation of NPs [15], especially when the histopathological assessment is not applicable due to it is not easy to obtain enough polyp tissue by biopsy before surgery [16].

In this study, we used peripheral eosinophilia as a marker for NPs with esinophilic infiltration, but we want to investigate the relation between peripheral eosinophil counts and severity of nasal polyps grades in AR patients and if this will predict the severity of the sinus disease.

Patient and methods

Study design

This study was conducted on 160 patients with allergic rhinitis (as proved by history and skin test) at the otorhinolaryngology department, university hospitals, over a period from January 2020 to January 2021. Informed consent was signed by all enrolled subjects or their relative after an explanation of the research purpose.

The exclusion criteria are patients under 18 years, patients who received steroids therapy or systemic antibiotics 1 month before enrollment in the study, patients with autoimmune disease, patients with recurrent nasal polypi after previous surgery, patients who has allergy elsewhere in the body or on medical treatment for allergy, and patients diagnosed with fungal rhinosinusitis, cystic fibrosis, primary ciliary dyskinesia, inverted papilloma, and any neoplastic lesions.

The following are the investigations:

- Full ENT examination.
- History taking.
- All included patients complained of a symptom of AR: at the clinical visit, the patients gave symptoms of nasal blockage, nasal itching, sneezing, and rhinorrhea.
- Each patient underwent CT examination of the nasal cavity and sinuses to predict patients with eCRSwNP; according to Lund-Mackay scoring system, Meng et al. [17] found that an optimal cutoff value of > 2.59 for the ethmoid sinus/maxillary sinus (E/M) CT score ratio demonstrated a sensitivity of 94% and a specificity of 90% for eCRSwN.
- Endoscopic examination to detect different grading of nasal polyps according to the Meltzer Clinical Scoring System [18] is a 0–4 nasal polyp grading system:

  0 = no polyps
  1 = polyps confined to the middle meatus
  2 = multiple polyps occupying the middle meatus
  3 = polyps extending beyond the middle meatus
  4 = polyps completely obstructing the nasal cavity

Blood samples were taken from every patient who fulfilled the inclusion criteria to detect absolute eosinophil counts.

The patients were compared as regards the demographic features (age and sex), associated anatomical variations and pathology, complications, and recurrence rate.

Statistical methods

All analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 15 packed programs. A difference was considered significant at $p < 0.05$.

Results

One hundred sixty patients were included in the current study and divided into two groups: first group—54 patients without nasal polyps (35 males and 19 females) with age ranging from 18 to 55 years (mean = 39.7 ± 11). Within 54 patients with no nasal polyps, eosinophil count ranged between 0.001×10^3 µl and 0.907×10^3 µl with a mean of 0.2399 (SD = 0.2153).

The second group included 106 patients with nasal polyps (65 males and 41 females); their age ranged between 19 and 76 years (mean = 41.7 ± 14.9), and eosinophil count ranged between 0.05×10^3 µl and 14.7×10^3 µl with a mean of 1.6645 = 3.06 with significant difference between the two groups ($p = 0.0008$, $t = 3.418$) (Tables 1 and 2).

In grade 1 (36 patients), eosinophil count ranged between 0.05×10^3 µl and 7.68×10^3 µl with a mean

Table 1 Comparison of group A (without polyps) and group B (with polyps)

Parameter	Group A (without polyp)	Group B (with polyp)	*P* value
Gender			
Male	35	65	0.666 ($X^2 = 0.186$)
Female	19	41	
Age (in years)			
Range	21–68	19–76	0.3379 ($t = 0.9612$)
Mean ± SD	39.7 ± 11	41.7 ±14.9	
Eosinophil count (in $\times 10^3$ µl)			
Mean ± SD	0.2399 ± 0.2153	1.6645 ± 3.06	< 0.0001 ($F = 9248$)
Range	0.001–0.907	0.7 + 14.7	

SD standard deviation, *X* chi-square test, *F* ANOVA test

Table 2 Comparison of the mean eosinophil count in different grades of the nasal polyps

Polyps grade	Eosinophil count, mean ± SD (in $\times 10^3$ µl)	*P* value
In grade 1	0.7 ± 1.7	$P = 0.0094$ ($F = 4.028$)
In grade 2	1.4588 ± 3.1296	
In grade 3	1.553 ± 0.3	
In grade 3	2.95595 ± 3.856	

SD standard deviation, *X* chi-square test, *F* ANOVA test

of 0.7 + 1.7. In grade 2 (18 patients), eosinophil count ranged between 0.117 × 10^3 µl and 10.3 × 10^3 µl with a mean of 1.4588 + 3.1296. In grade 3 (14 patients), eosinophil count ranged between 0.114 × 10^3 µl and 0.986 × 10^3 µl with a mean of 0.553 + 0.3. In grade 4 (38 patients), eosinophil count ranged between 0.132 × 10^3 µl and 14.7 × 10^3 µl with a mean of 2.95595 + 3.856 (Table 2).

The difference between grades was found statistically highly significant ($p < 0.0001$, ANOVA, $F = 9248$).

Post hoc test: polyp grade1 1 vs grade 2—Diff = 0.7588, 95%CI = −1.3777 to 2.8953, $p = 0.7901$; polyp grade 1 vs grade 3—Diff = −0.1470, 95%CI = −2.4781 to 2.1841, $p = 0.9983$; polyp grade 1 vs grade 4—Diff = 95,594.3000, 95%CI = 95,592.5787 to 95,596.0213, $p = 0.0000$; polyp grade 2 vs grade 3—Diff = −0.9058, 95%CI = −3.5431 to 1.7315, $p = 0.8064$; polyp grade 2 vs grade 4—Diff = 95,593.5412, 95%CI = 95,591.4236 to 95,595.6588, $p = 0.0000$; and polyp grade 3 vs grade 4—Diff = 95,594.4470, 95%CI = 95,592.1332 to 95,596.7608, $p = 0.0000$.

Discussion

Fokkens et al. [6] in the European Position Paper (EPOS) published in 2020 described an association between asthma and CRS; eosinophilia and asthma are risk factors for CRSwNP and disease recurrence. Eosinophilia affects the respiratory function and is associated with greater disease severity and recurrence rates [19] and hence severe sinus disease.

About 24 years ago, Hellquist [20] reported that eosinophilic polyps accounted for 86% of all polyps in Sweden. Ishitoya et al. [21] divide CRSwNP into two types, eosinophilic chronic rhinosinusitis (ECRS) and non-ECRS. Ferguson [22] and Orlandi [23] subclassified ECRS into 4 groups: superantigen-induced ECRS, classic allergic fungal rhinosinusitis (AFRS), non-allergic fungal ECRS, and aspirin-exacerbated ECRS. Know the term "eosinophilic CRSwNP" is used rather than ECRS which indicates more tissue eosinophilic infiltration.

Therefore, eosinophils are the most common and important inflammatory cells in the pathogenesis of polyps [24, 25]. To diagnose this type of NPs, tissue biopsy is the gold standard. However, to assess the severity of the sinus disease, diagnosis must occur preoperatively. It is not always easy to take enough biopsies from the nose preoperatively due to poor patient compliance [16], besides taking serial biopsies to diagnose, follow-up, and predict the recurrence is coasty.

In addition, a biopsy cannot be taken after FESS and clearance of sinuses from polyp; so to follow up and to pick up recurrence, more time must pass until polyps appear again to be detected by CT or tissue histopathology.

Several studies proved that peripheral eosinophilia is strongly correlated to tissue infiltration with eosinophils in CRSwNP [21, 26–28]. Our results support these studies as we found a positive correlation between peripheral eosinophil counts and the presence of nasal polyps; the eosinophil counts were lower in CRSsNP patients.

A recent study demonstrated that the specificity of peripheral eosinophils as a predictor for the diagnosis of eCRSwNP was only 75.3% [29]. In this regard, CT has more specificity by using Lund-Mackey scores with a specificity of 90% [17] or Japanese Epidemiological Survey of Refractory Eosinophilic Chronic

Rhinosinusitis (JESREC) with a specificity of 66% [30]. In our opinion, specificity of CT could be affected by the improper reading of sinus shadow and whether the patient underwent previous sinus surgery or not. Even if, the specificity of peripheral eosinophilia is quite similar to CT especially when excluding other causes of peripheral eosinophilia.

The blood eosinophil count could be a good marker for the eosinophilic inflammation of NPs. All these data suggested that the occurrence of eosinophilic NPs was closely related to allergy. However, the role of allergy in the pathogenesis of NPs is still controversial. A few studies have questioned the role of allergy in the pathogenesis of NPs. After evaluating 3000 atopic patients, it was found that only 0.5% of patients had NPs [31]. Other reports were also unable to support either a higher incidence of atopy in patients with NPs or a pattern of allergic inflammation in the pathogenesis of NPs [32–34]. Thus, the present study requires further validation by studies with a larger sample size. It was also found that eosinophil infiltration was directly correlated with disease severity, since both total and each item's score were higher in eosinophilic NPs; also, the peripheral eosinophil count was directly proportionate with the severity of nasal polyp grade; the eosinophil counts were high in grade 3 and 4 nasal polyps. Besides, higher Lund-Kennedy and Lund-Mackey scores in eosinophilic NPs were also found. Taken together, these results suggest that eosinophilic NPs predict long disease duration and poor prognosis.

So, eosinophil is part of the nasal polypi disease, and its level significantly increases on increasing polyp grading (severity), so it could be suggested to be a simple easy and available and repeatable indicator for nasal polypi servility and may recurrence and this need to be investigated after nasal surgery for nasal polyposis and in recurrent cases. It could be also used as an indicator of medical treatment efficiency even before polyps appear.

So, a basal level of the patient's eosinophil should be available on the first visit to reassess. Thus, we in agree with Aslan et al. [35] that peripheral eosinophilia can be used as an easy, safe, and reliable marker to predict disease severity in nasal polyps. So, this investigation is safe, reliable, easily applicable, and cost-effective, and blood samples could be obtained from both outpatient and hospitalized patients and can be done even by a general practitioner to predict the severity of sinus disease preoperative and to follow-up patients postoperative and pickup early recurrence. It is recommended to be investigated on larger series of patients with a longer follow-up period.

Conclusion

Measuring peripheral eosinophil counts is simple, low cost, safe, and directly proportionate with different grades of nasal polyps. It can be used as a reliable marker to predict the severity of nasal polyps and consequently predict the prognosis of sinus disease and quality of life.

Abbreviations

CRS: Chronic rhinosinusitits; CRSsNP: CRS without NPs; CRSwNP: CRS with NPs; NPs: Nasal polyps; Th2T: Helper 2.

Acknowledgements

Not applicable.

Authors' contributions

MWE suggested and modified the idea, reviewed the literature, designed the study and concept, revised the results, did the statistical analysis, interpreted the data, tabulate the interpreted data, wrote and revised the article, and approved the final manuscript to be published. MAM developed the idea, collected the data, tabulated the data, kept the patient records, analyzed the data, revised the article, and contributed to the final approval of the article. EH developed the research idea, reviewed the literature, contributed to the data interpretation, revised the manuscript, and contributed to the final approval of the article. All authors have read and approved the final manuscript.

Funding

None; the authors declare no financial support or interest in this study.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Written informed consent was obtained from the study participants, and Zagazig University IRB approved the study proposal (IRB 117-1-18).

Consent for publication

Not applicable (no images or videos related to participants).

Competing interests

The authors declare that they have no competing interests.

Received: 5 May 2022 Accepted: 23 June 2022
Published online: 15 July 2022

References

1. Stevens WW, Schleimer RP, Kern RC (2016) Chronic rhinosinusitis with nasal polyps. J Allergy Clin Immunol Pract 4(4):565–572
2. Fokkens W, Lund V, Mullol J (2007) EP3OS 2007: European Position Paper on rhinosinusitis and nasal polyps 2007. A summary forotorhinolaryngology. Rhinology 45:97–101
3. Bachert C, Zhang L, Gevaert P (2015) Current and future treatment options for adult chronic rhinosinusitis: focus on nasal polyposis. J Allergy Clin Immunol 136(6):1431–1440
4. Fokkens WJ, Lund VJ, Mullol J et al (2012) EPOS 2012: European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists. Rhinology 50(1):1–12
5. Orlandi RR, Kingdom TT, Hwang PH et al (2016) International consensus statement on allergy and rhinology: rhinosinusitis. Int Forum Allergy Rhinol 6(Suppl 1):S22–S209
6. Fokkens WJ, Lund VJ, Hopkins C et al (2020) European Position Paper on chronic rhinosinusitis and nasal polyps 2020. Rhinol Suppl 58:1–464

7. Dennis SK, Lam K, Luong A (2016) A review of classification schemes for chronic rhinosinusitis with nasal polyposis endotypes. Laryngoscope Investig Otolaryngol 1(5):130–134
8. Liu JX, Liao B, Yu QH et al (2020) IL-37-Mex3B-TLR3 axis in epithelial cells in eosinophilic chronic rhinosinusitis with nasal polyps. J Allergy Clin Immunol 145(1):160–172
9. Ricciardolo F, Sorbello V, Folino A et al (2017) Identification of IL-17F/ frequent exacerbator endotype in asthma. J Allergy Clin Immunol 140(2):395–406
10. Tosun F, Arslan HH, Karslioglu Y, Deveci MS, Durmaz A (2010) Relationship between postoperative recurrence rate and eosinophil density of nasal polyps. Ann Otol Rhinol Laryngol 119:455–459
11. Cao PP, Li HB, Wang BF et al (2009) Distinct immunopathologic characteristics of various types of chronic rhinosinusitis in adult Chinese. J Allergy Clin Immunol 124:478–484
12. Tomassen P, Vandeplas G, Van Zele T et al (2016) Inflammatory endotypes of chronic rhinosinusitis based on cluster analysis of biomarkers. J Allergy Clin Immunol 137:1449–1456.e4
13. Kim JW, Hong SL, Kim YK, Lee CH, Min YG, Rhee CS (2007) Histological and immunological features of non-eosinophilic nasal polyps. Otolaryngol Head Neck Surg 137:925–30.9
14. Avord ID, Brightling CE, Woltmann G, Wardlaw AJ (1999) Non-eosinophilic corticosteroid unresponsive asthma. Lancet 353:2213–4.11
15. Sun C, Ouyang H, Luo R (2017) Distinct characteristics of nasal polyps with and without eosinophilia. Braz J Otorhinolaryngol 83:66–72
16. Wang E, Zheng Y, Liu P et al (2014) Eosinophilic chronic rhinosinusitis in East Asians. World J Clin Cases 2:873–882
17. Meng Y, Lou H, Wang C, Zhang L (2016) Predictive significance of computed tomography in eosinophilic chronic rhinosinusitis with nasal polyps. Int Forum Allergy Rhinol 6:812–819. https://doi.org/10.1002/alr.21749
18. Meltzer EO, Hamilos DL, Hadley JA et al (2006) Rhinosinusitis: developing guidance for clinical trials. J All Clin Immun 118:17–61
19. Chen S, Zhou A, Emmanue B, Thomas K, Guiang H (2020) Systematic literature review of the epidemiology and clinical burden of chronic rhinosinusitis with nasal polyposis. Curr Med Res Opin 36(11):1897–1911
20. Hellquist HB (1996) Nasal polyps update. Histopathology. Allergy Asthma Proc 17:237–242
21. Ishitoya J, Sakuma Y, Tsukuda M (2010) Eosinophilic chronic rhinosinusitis in Japan. Allergol Int 59:239–245
22. Ferguson BJ (2004) Categorization of eosinophilic chronic rhinosinusitis. Curr Opin Otolaryngol Head Neck Surg 12:237–242
23. Ferguson BJ, Orlandi RR (2006) Chronic hypertrophic rhinosinusitis and nasal polyposis. In: Bailey BJ, Johnson JT, Newlands SD (eds) Head and neck surgery–otolaryngology. Lippincott Williams & Wilkins, Philadelphia, pp 394–399
24. Bernstein J (2001) Nasal polyps. In: Kennedy DW, Bolger WE, Zinreich SJ (eds) Diseases of the sinuses: diagnosis and management. B.C. Decker Inc., London, pp 69–75
25. Armengot M, Garin L, Carda C (2009) Eosinophil degranulation patterns in nasal polyposis: an ultrastructural study. Am J Rhinol Allergy 23:466–470
26. Kim JW, Hong SL, Kin YK et al (2007) Histological and immunological features of non-eosinophilic nasal polyps. Otolaryngol Head Neck Surg 137:925–930
27. Kountakis SE, Arango P, Bradley D, Wade ZK, Borish L (2004) Molecular and cellular staging for the severity of chronic rhinosinusitis. Laryngoscope 114:1895–1905
28. Ikeda K, Shiozawa A, Ono N et al (2013) Subclassification of chronic rhinosinusitis with nasal polyp based on eosinophil and neutrophil. Laryngoscope 123:E1–E9
29. Hu Y, Cao P, Liang G et al (2012) Diagnostic significance of blood eosinophil count in eosinophilic chronic rhinosinusitis with nasal polyps in Chinese adults. Laryngoscope 122:498–503
30. Lou H, Zhang N, Bachert C, Zhang L (2018) Highlights of eosinophilic chronic rhinosinusitis with nasal polyps in definition, prognosis, and advancement. Int Forum Allergy Rhinol 8:1218–1225
31. Caplin I, Haynes JT, Spahn J (1971) Are nasal polyps an allergic phenomenon? Ann Allergy 29:631–634
32. Drake-Lee AS (1989) Nasal polyps. In: Mackay IS (ed) Rhinitis: mechanism and management. Royal Society of Medicine, London, pp 141–152
33. Bachert C, Gevaert P, Holtappels G, van Cauwenberge P (2002) Media-tors in nasal polyposis. Curr Allergy Asthma Rep 2:481–7.24
34. Baroody FM, Hughes CA, McDowell P, Hruban R, Zinreich SJ, Naclerio RM (1995) Eosinophilia in chronic childhood sinusitis. ArchOtolaryngol Head Neck Surg 121:1396–1402
35. Aslan F, Altun E, Paksoy S, Turan G (2017) Could Eosinophilia predict clinical severity in nasal polyps? Multidiscip Respir Med 12(21):1–5

Publisher's Note