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Nasal Eosinophilia for Diagnosing Allergic Rhinitis: A Diagnostic Accuracy Study in Yaoundé-Cameroon

Valeur diagnostique de l'éosinophilie nasale dans le diagnostic de la rhinite allergique à Yaoundé-Cameroun

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ABSTRACT

Background. Previous studies have suggested that nasal eosinophilia could be used as an alternative to skin prick test for diagnosing allergic rhinitis. The aim of the present study was to evaluate the performance of nasal eosinophilia in the diagnosis of allergic rhinitis in Yaounde. **Methods.** Fifty-two patients (7-51 years old, 35 women) presenting recurrently or permanently at least two rhinological signs among rhinorrhea, sneezing and nasal obstruction were cross-sectionally included in the study. They were classified as allergic rhinitis and non-allergic rhinitis according to their reaction to 9 allergens (ALK-Abelló®) on skin prick test (gold standard). Nasal secretion swabs for eosinophil quantification were performed concomitantly in all patients. A double entry contingency table was established for the calculation of nasal eosinophilia performance indices for the diagnosis of allergic rhinitis. **Results.** Forty patients (77%) had allergic rhinitis. House dust mites were the most common allergens. Nasal eosinophilia was noted in 15 patients with an average of 19.2 eosinophils per 100 cells counted. The sensitivity, specificity, positive predictive value and negative predictive value of nasal eosinophilia were 37.5%, 75%; 83.3% and 26.4% respectively. The positive and negative likelihood ratio was 1.5 and 0.5 respectively. The Youden index was 0.125. There was no cut-off value for nasal eosinophilia that improved its sensitivity and specificity. **Conclusion.** The performance of nasal eosinophilia in the diagnosis of allergic rhinitis is poor. It is not very sensitive and moderately specific, and therefore cannot be used in the diagnostic strategy of allergic rhinitis in our milieu.

RÉSUMÉ

Introduction. Selon plusieurs études**,** l'éosinophilie nasale pourrait être utilisée comme alternative aux tests cutanés pour le diagnostic de la rhinite allergique. Le but de notre étude était ainsi d'évaluer la performance de l'éosinophilie nasale dans le diagnostic de la rhinite allergique à Yaoundé. **Méthodes.** Cinquante-deux patients (7-51 ans, 35 femmes) présentant de manière récurrente ou permanente au moins deux signes rhinologiques parmi la rhinorrhée, les éternuements et l'obstruction nasale ont été inclus transversalement dans l'étude. Ils ont été classés en rhinite allergique et non allergique selon leur réaction à 9 allergènes (ALK-Abelló®) au test cutané allergique (gold standard). Des prélèvements de sécrétions nasales pour la quantification des éosinophiles ont été réalisés simultanément. Des indices de performance de l'éosinophilie nasale pour le diagnostic de la rhinite allergique ont été calculés. **Résultats.** Quarante patients (77 %) avaient une rhinite allergique. Les acariens étaient les allergènes les plus courants. Une éosinophilie nasale a été notée chez 15 patients avec une moyenne de 19,2 éosinophiles/100 cellules comptées. La sensibilité, la spécificité, la valeur prédictive positive et la valeur prédictive négative de l'éosinophilie nasale étaient de 37,5 %, 75 % ; 83,3 % et 26,4 % respectivement. Le rapport de vraisemblance positif et négatif était respectivement de 1,5 et 0,5. L'indice de Youden était de 0,125. Il n'y avait pas de valeur seuil pour l'éosinophilie nasale qui améliorait sa sensibilité et sa spécificité. **Conclusion.** Les performances de l'éosinophilie nasale dans le diagnostic de la rhinite allergique sont médiocres. Elle est peu sensible et moyennement spécifique, et ne peut donc pas être utilisée dans la stratégie diagnostique de la rhinite allergique dans notre milieu.

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HIGHLIGHTS

What is already known on this topic

Nasal smear eosinophilia is accepted as a useful finding in the diagnosis of allergic rhinitis (AR), although not pathognomonic. Its validity and reliability are not clear making it hardly ever performed in the diagnosis of AR.

What question this study addressed

The diagnostic performance of nasal eosinophilia versus SPT for diagnosing allergic rhinitis in Yaounde.

What this study adds to our knowledge

Nasal eosinophilia is a mediocre tool for diagnosing allergic rhinitis in our setting

How this is relevant to practice, policy or further research.

The absence of nasal eosinophilia doesn't allow to exclude allergic rhinitis in our context.

INTRODUCTION

Allergic rhinitis (AR) is the set of functional nasal manifestations caused by the development of immunoglobulin E (IgE)-dependent inflammation of the nasal mucosa in response to exposure to different types of allergens[1]. It is one of the most widespread chronic diseases in the world, affecting all ages with a prevalence of 10 to 54% [2]. It has a significant impact on quality of life, constituting a real public health issue [3].

The fact that the prevalence of AR varies so much between epidemiological studies is mainly due to the lack of diagnostic standardization [4]. Indeed, there are many ways to diagnose AR. Although the gold standard remains the skin prick tests (SPT) [5], some authors have suggested that nasal smear esosinophilia could be helpful in diagnosing AR. Sanli et al for example in Istanbul, comparing the usefulness of nasal smear eosinophilia with SPT for the diagnosis of AR, found that both tests showed good correlation with clinical history [6]. Analogously, Annesi-Maesano I et al in France in 2002, developed a "Score for Allergic Rhinitis" (SFAR) proposed to be useful in estimating prevalence and to study causation of AR in population settings [7].

In the Cameroonian health environment, where the reported prevalence of allergic rhinitis is 11.4% [8], SPT are not available in public hospitals. They remain the prerogative of reference or private laboratories and are therefore not very affordable. In this context, in order to compensate for this lack, it appears necessary to set up a less complex diagnostic protocol for AR. Nasal smear eosinophilia, which is simple to perform, non-invasive, inexpensive, useable at any age and without risk of anaphylactic reaction, would seem to be a good alternative in this purpose [9].

Therefore, we sought through this study to evaluate the diagnostic performance of nasal eosinophilia versus SPT for diagnosing allergic rhinitis in Yaounde.

METHODS

Study design

We performed a paired-reader, paired-patient diagnostic accuracy study

Study setting and population

The study was conducted from August to December 2019 (5 months) in the five 1st and 2nd category university hospitals in Yaounde ie Central Hospital, Gyneco-obstetric and pediatric Hospital, University teaching Hospital, General Hospital and Essos Hospital Center.

Patients who had recurrently or permanently since 1 year, at least two of the three rhinological symptoms amidst clear anterior rhinorrhoea, nasal obstruction and sneezing; where included. We excluded those patients with a condition that could interfere with the performance of SPT or nasal mucosa sampling (ongoing systemic or local antihistaminic or corticosteroid treatment, skin dermatosis of the forearms, gravidic amenorrhoea...).

Variables

The variables of study were age, sex, SPT results and nasal eosinophilia. Patients with a positive SPT to one or more allergens were considered having AR.

Sample size

The sampling was consecutive and non-probabilistic. The minimal sample size, calculated from the prevalence of AR (11.4% [8]) with a precision of 10% and a risk of error of 5%, was 35 patients.

Data resource and measurement

Demographic variables (sex, age) SPT and nasal eosinophilia result were collected in a predefined form.

The SPT was performed on the anterior part of the patient's forearm. After degreasing the skin with alcohol and drying it, a drop of each allergenic extract, identified by a specific marking, was placed on the skin at an interval of at least three centimeters between each drop. Using a staller point grasped between the thumb and forefinger, a puncture transfixing the dermis was made through the drop. A new staller point was used for each drop. Tests with positive and negative control solutions were performed at the same time and according to the same principle to eliminate dermographism. The reading was done after 20 minutes by measuring the diameter of the generated papule. A diameter ≥ 3 mm accompanied by pruritus and/or erythema was considered a positive reaction. Allergenic extracts from the ALK-Abelló® laboratory were used. These were *Histamine Hydrochloride Solution*, batch no. 00010281 38-100 IR (positive control reagent); *Glycerosaline Solution*, batch no. 00010251 38-100 IR (negative control reagent); Pneumallergens including extracts of *Acarian mix*, batch no. 00010241 38-100 IR; *Mould (Altenaria alternata)*, batch no. 0001115041-100 IR ; *cat dander*, batch no. 0001032831-100 IR; *dog dander*, batch no. 0001153429-100 IR; corn pollen, batch no. 0001024133-100 IR; and trophallergens including *Peanut extract*, batch no. 0000903217-100 IR; *soybean extract*, batch no.

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0000848977-100 IR; *egg white*, batch no. 0000903219-100 IR; and *egg yolk*, batch no. 0000844197-100 IR.
For nasal cytology, nasal secretions were collected by sterile swabbing (one in each nostril) from the lower turbinate and then spread on a slide. The slide was air-dried for 5 minutes then fixed with 95° alcohol and stained with May-Grunwald-Giemsa. Inflammatory cells were counted at high magnification (x 100) with immersion oil. The slides were read in the anatomy and cytopathology laboratory of the gynaeco-obstetric and pediatric hospital in Yaounde by a cytotechnician and the results validated by an anatomo-cytopathologist. The count of each type of cell was determined per 100 cells counted

Data analysis

SPSS® 24.0 (IBM, Chicago, Illinois) software was used for statistical analysis. Quantitative variables were represented by their measure of central tendency and dispersion, namely, mean ± standard deviation, mode, median and range. Categorical variables were expressed as percentages. The comparison of percentages was performed by the chi-square test. Comparison of means was performed by Student's t-test or one-way analysis of variance (ANOVA). The diagnostic value of nasal cytology compared with SPT was assessed by calculating its sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive and negative likelihood ratio and Youden index. All significance tests were two-sided and probability values of $p<0.05$ were considered statistically significant.

Ethical considerations

From an ethical point of view, a favorable opinion from the ethics committee of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I was obtained, as well as authorizations from the various hospitals concerned. Patients signed an informed consent form and were not paid for their participation. The tests were carried out free of charge.

RESULTS

Presentation of the study population

A total of 64 patients were seen during the study period and only 52 of them were included (Figure 1).
A positive reaction to at least one allergen was found in 40 patients [(mean age of 25.4 ± 11.6 years (7 to 51 years), 27 women] giving a prevalence of allergic rhinitis of 77%. Table I presents the demographic characteristics of the study population.

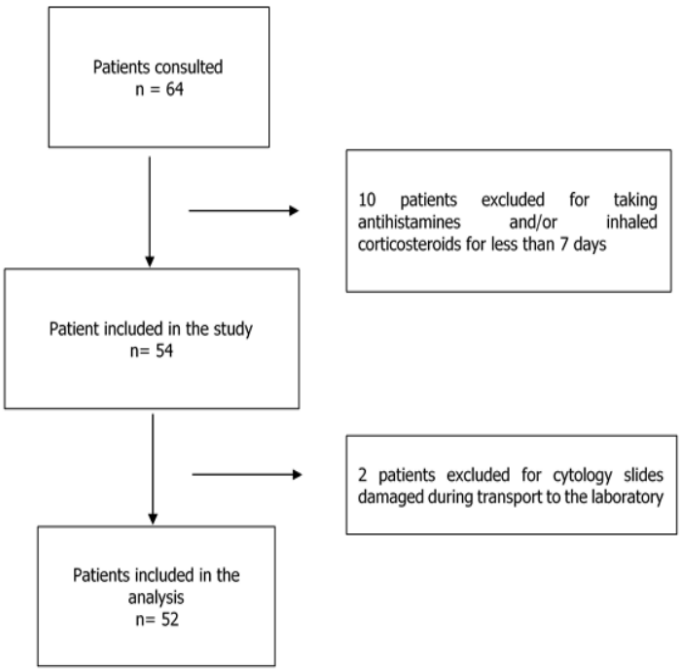

Figure 1 : Flow chart of the study population

Table I: Demographic characteristics of the study population

	AR (n=40)	NAR (n=12)
Age (YEARS)		
≤ 20	14 (35%)	3 (25%)
21-40	22 (55%)	8 (66.7%)
40+	4 (10%)	1 (8.3%)
Gender		
Male	13 (32.5%)	4 (33.3%)
Female	27 (67.5%)	8 (66.7%)

AR : Allergic Rhinitis ; NAR : Non Allergic Rhinitis

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Table II: Nasal cytology results in the study population

	AR (n=40)			NAR (n=12)			*p*
	Mean	ST	95%CI	Mean	ST	95%CI	
Eosinophil*	19.2	28.79	[10- 28.4]	15,92	31,87	[-4.33– 36.17]	0.73
Neutrophil*	52.75	41.85	[39.3– 66.14]	48,17	49,74	[16,56– 79,77]	0.75
Basophil*	.00	.00	/	.00	.00	/	/
Monocyte*	0.1	0.38	[-0.02– 0.22]	0,08	0.29	[-0.1– 0.27]	0.88
Lymphocyte*	0.48	1.77	[-0.01– 1.04]	0,00	.00	/	0.36

ST : Standard Deviation, AR : Allergic Rhinitis ; NAR : Non Allergic Rhinitis
* Units in number of cells per 100 leukocytes counted

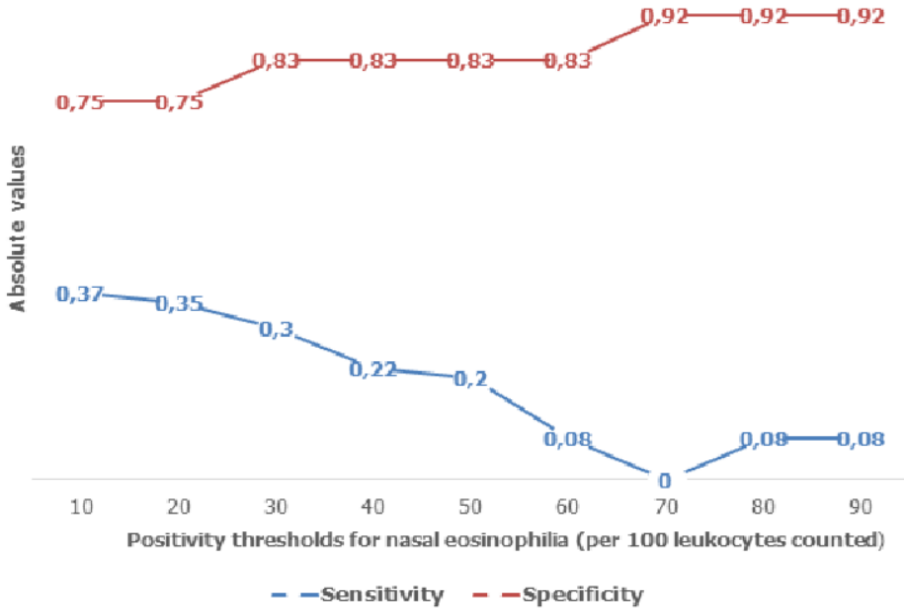

Figure 2: Sensitivity and specificity curves for nasal eosinophilia at different thresholds of positivity

Results of SPT

These patients were predominantly sensitive to pneumallergens, with *Acarian mix* being the main one, reactive in 29 (72.5%) patients, followed by mould, reactive in 19 patients (47.5%), and corn pollen in 17 patients (42.5%) Peanut was the main trophallergen, reactive in 16 patients (40%). Sensitization to more than one allergen was present in 26 (65%) patients.

Results of nasal cytology

The mean level of eosinophils in nasal secretions was higher in the AR than the non-AR population, although the difference was not statistically significant (19.2 vs 15.92; p=0.737) as shown in Table II.

Diagnostic value of nasal eosinophilia in allergic rhinitis

Amongst patients with AR, nasal smear eosinophilia was positive in 15 of them, whilst only 3 patients without AR had positive nasal eosinophilia.

Therefore the sensitivity, specificity, PPV and NPV of nasal eosinophilia for the diagnosis of allergic rhinitis were 37.5%, 75%; 83.3%; 26.4% respectively. The positive and negative likelihood ratios were 1.5 and 0.5 respectively. The Youden index was 0.125.

There was no cut-off value for nasal eosinophilia, which concomitantly improves its sensitivity and specificity in the diagnosis of allergic rhinitis as illustrated in figure 2.

DISCUSSION

SPT and RAST remain a luxury in our practice. However, the determination of the allergic character of chronic rhinological symptoms is crucial in order to implement allergenic eviction measures. Therefore, in order to alleviate the inaccessibility of these reference tests, we wanted to evaluate the diagnostic performance of an alternative that appeared simple and minimally invasive ie nasal eosinophilia.

Our sample consisted of 52 patients with suspected AR. Of these, 77% were sensitive to at least one allergen. Mites, molds and peanuts, which cross-allergy with grasses is well known, were the most common allergens, similar to the findings in the literature. [10]. The authors specify that this is the prevalence among chronic rhinitis patients and not the prevalence in the general population. Thus, this prevalence differs from that described in the literature, which varies between 10 and 54% [2, 4, 8]. Nevertheless, among these allergic patients, there was a predominance of young people (25 years old on average) and women (sex ratio M: F of 2:1); a trend found by several authors [11, 12]. Rosario et al [13] made the hypothesis of the role of female sex hormones, but also of different lifestyles adopted by men and women, microbiota diversity, diet distinctions, professional options, and adherence to treatment, among others to explain this tendency.

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For the collection of nasal secretions for the quantification of nasal eosinophilia we used the swabbing method, a technique that is not very restrictive and can be performed at any age. Nasal cavity washing with centrifugation of the collected secretions [14], brushing of the lower turbinates, the gelatin impression method [15] or nose blowing [16] were not used because they require specific equipment that is not available in current practice, making them inappropriate for the present study.

The mean level of eosinophils in nasal secretions was thereby higher among AR patients although the difference was not statistically significant in this study. These results are corroborated by different authors [17, 18]. Indeed, infiltration of tissue by various inflammatory cells (including eosinophils and neutrophils) is the characteristic feature of the late-phase reaction of allergy which is set in 2 to 24 hours after initial exposure and may last for several days. However, eosinophilia in nasal smear in AR raises the issue of the differential with non-allergic rhinitis with eosinophilic syndrome (NARES) which is also a chronic inflammation of the nasal mucosa (> 20% of eosinophils in nasal cytology) in the absence of demonstrable allergy (negative in vivo and in vitro tests); often accompanied by other sinonasal conditions (nasal polyposis, chronic rhinosinusitis) [19]

In terms of performance, this study showed that nasal eosinophilia is not very sensitive, moderately specific and has a high PPV due to the high prevalence of allergic rhinitis in the study population. This relative specificity of nasal eosinophilia in the diagnosis of AR is widely reported by authors. This specificity was 100% for a sensitivity of 62% in a study by Pal I et al [17], 76% in a study by Takwoingi Y et al [20] or 71.2% in a study by Qamar S et al [18]. This specificity of nasal eosinophilia would have been of interest if the aim of the diagnostic process here was to affirm or confirm the diagnosis and the risk of a false positive result was substantial and unacceptable. However, given that allergic rhinitis is a fairly prevalent disease, the aim of the diagnostic process here is to exclude the disease, which is even more controllable if treated early. It is consequently a sensitive test that would have been interesting as an alternative to the SPT [21]. Furthermore, irrespective of the prevalence of allergic rhinitis in the population, the positive (1.5) and negative (0.5) likelihood ratios of nasal eosinophilia were very low in the present study, suggesting little or no effect and no usefulness in the diagnosis of allergic rhinitis [22]. Consequently, eosinophilia in our opinion cannot be used as an efficient alternative to SPT in the diagnosis of AR

A French team [7] proposed in 2002 a clinical score : the SFAR ; with a sensitivity, specificity, PPV and NPV of 74%, 83% , 84% and 74% respectively that would appear to be useful to estimate prevalence and to study causation of AR in population settings. It would be interesting to carry up a diagnostic accuracy study of such a score in our context to verify its applicability as an alternative to SPT for diagnosing AR.

Notwithstanding the small sample size, we were also limited by the number of allergens to be tested during SPT. Moreover, by using more sophisticated nasal sampling techniques, we might have had a greater number of patients with eosinophilia or a higher rate of eosinophils in the latter. A study on a larger sample of patients with chronic rhinitis, with a more extensive SPT allergens range and nasal sampling by washing/centrifugation could therefore refine our results.

CONCLUSION

The present study shows that eosinophil count in nasal smears is a moderately specific criterion for the diagnosis of AR with a 83% positive predictive value. Its sensitivity is somewhat lower at 37.5%. Furtherance, there is no cut-off value of eosinophilia that enhance its performance. Considering its very weak positive and negative likelihood ratio, we can say that nasal eosinophilia is a mediocre tool for diagnosing RA in our setting and therefore we don't recommend it as a routine test in daily practice.

Competing interests

The authors declare no competing interest.

Authors' contributions

LC Atanga designed the study protocol, and statistical analysis and wrote the manuscript ; C Ndassa- conceived the study and wrote the manuscript, E Choffor provided critical insights ; R Meva'a, E Choffor, R Njock and F Djomou reviewed and contributed to the final written manuscript

REFERENCES

1.Braun J J, Devillier P , Wallaert B, Rancé F, Jankowski R, Acquavita J-L, Beley G, Demoly P. Recommandations pour le diagnostic et la la prise en charge de la rhinite allergique (épidémiologie et physiopathologie exclues) - texte long Revue française d'allergologie. 2010;27:79-105.

2.Skoner D. Allergic rhinitis: definition,epidemiology,pathophysiology, detection and diagnosis. Journal of Allergy and Clinical Immunology. 2001;108(1):2-8.

3.Bousquet J, Van Cauwenberg P, Khaltaev N, ARIA workshop group, World Health Organization. Allergic rhinitis and its impact on asthma. The Journal of allergy and clinical immunology. 2001;108(5):147-334.

4.Bernstein DI, Schwartz G, Bernstein JA. Allergic Rhinitis: Mechanisms and Treatment. Immunol Allergy Clin North Am. 2016 ; 36 (2):261-78.

5.Schwartz DA. Gene-environment interactions and airway disease in children. Pediatrics. 2009;123(3):151-9.

6.Sanli A, Aydin S, Ateş G, Eken M, Celebi O. Comparison of nasal smear eosinophilia with skin prick test positivity in patients with allergic rhinitis. Kulak Burun Bogaz Ihtis Derg. 2006;16(2):60-3.

7.Annesi-Maesano I, Didier A, Klossek M, Chanal I, Moreau D, Bousquet J. The score for allergic rhinitis (SFAR): a simple and valid assessment method in population studies. Allergy. 2002; 57(2):107-14.

8. Pefura-Yone EW, Kengne AP, Balkissou AD, et al. Prevalence of asthma and allergic rhinitis among adults in Yaounde, Cameroon. PLoS One. 2015;10(4):e0123099. doi:10.1371/journal.pone.0123099

9.Gelardi M IC, Passalacqua G, Quaranta N, Frati F. The classification of allergic rhinitis and its cytological correlate. Allergy. 2011; 66:1624–5.

10. Tantilipikorn P, Pinkaew B, Talek K, Assanasen P, Triphoon Suwanwech TS, Bunnag C. Pattern of allergic

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sensitization in chronic rhinitis: A 19-year retrospective study. Asian Pac J Allergy Immunol. 2021;39(3):156-162.
11. Ciprandi G, Alesina R, Ariano R, Aurnia P, et al. Characteristics of patients with allergic polysensitization: the POLISMAIL study. European annals of allergy and clinical immunology. 2008;40(3):77-83.
12. Bellonti J A, Wallerstedt DB. Allergic rhinitis update: Epiddemiology and nature history. Allergy Asthma Proceedings. 2000;21(6):367-70.
13. Rosário CS, Cardozo CA, Neto HJC, Filho NAR. Do gender and puberty influence allergic diseases? Allergol Immunopathol (Madr). 2012 ;49(2):122-125.
14. Naclerio R, Proud D, Togias A. Inflammatory mediators in late antigen-induced rhinitis. New England Journal of Medicine. 1985;313:65-9.
15. Pipkorn U, Enerback L. A method for the preparation of inprints from the nasal mucosa. Journal of immunological methods. 1984;73:133-7.
16. Pelikan Z, Pelikan Filipek M. Cytologic changes in the nasal secretions during the immediate nasal response. Journal of Allergy and Clinical Immunology. 1988;82:1103-12.
17. Pal I, Sinha Babu A, Halder I, Kumar S. Nasal smear eosinophils and allergic rhinitis. Ear Nose Throat J. 2017; 96 (10-11):17-22.
18. Qamar S, Awan N, Cheema KM, Raza N, Ashraf S, Rehman A. Comparative Analysis of Nasal Smear Eosinophilia and Serum IgE Levels for the Diagnosis of Allergic Rhinitis. J Coll Physicians Surg Pak. 2020 ;30 (12):1297-1300.
19. Collado-Chagoya R, Hernández-Romero J, Eliosa-Alvarado GA, et al. Non-allergic rhinitis with eosinophilic syndrome. Case report. Rev Alerg Mex. 2018;65(3):310-315.
20. Takwoingi Y, Akang E, Nwaorgu G, Nwawolo C. Comparing nasal secretion eosinophil count with skin sensitivity test in allergic rhinitis in Ibadan, Nigeria. Acta Otolaryngol. 2003;123(9):1070-4.
21. Nendaz M.R., Perrier A. Sensibilité, spécificité, valeur prédictive positive et valeur prédictive négative d'un tes diagnostique. Rev mal respir. 2004 ; 21 : 390-3.
22. Delacour H., François N., Servonnet A., Gentile A., Roche B. Les rapports de vraisemblance : un outil de choix pour l'interprétation des test biologiques. Immunoanalyse et biologie spécialisée. 2009 ; 24 : 92-99.

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