The role of nasal cytology in the diagnosis of allergic and non-allergic rhinitis in adult and children

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Abstract. – OBJECTIVE: Chronic rhinitis is a common disease with an incidence of 40% in the Western population. Allergic rhinitis (AR) affects half of the adult population, while in children prevalence of AR vs. non-allergic rhinitis (NAR) of 3-4:1 is reported. Nasal cytology is the diagnostic test that has made it possible to clarify the cellular population of the nasal mucosa. The aims of the present study were to define the distribution of chronic rhinopathy in adult and pediatric populations, to classify "cellular" NAR into subgroups based on cytological features, and to identify overlapped rhinitis (OR).

PATIENTS AND METHODS: A retrospective study was conducted on 907 patients, divided into two groups: 135 children (69 females and 66 males, average age 9.8 years (range 4-17) and 772 adults (392 females and 380 males, average age 45.28 years (range 18-90). All patients with a suspicion of rhinopathy were submitted to nasal endoscopy, Skin Prick test (SPT), dosage of serum specific IgE, CT scan of nasal, and sinusal structures when chronic rhinosinusitis was suspected.

RESULTS: In the adult population of the study, 61% presented a diagnosis of chronic rhinitis: 213 patients (45.2%) had AR, 31 (6.6%) OR, and 227 (48.2%) NAR (77.5% of these patients presented a pattern of "cellular" NAR). In the pediatric population, 83% patients presented a rhinopathy: 61 (54.5%) with AR, 38 (34%) with NAR, and 13 (11.5%) with OR. Within the NAR group, 71% had a "cellular" pattern.

CONCLUSIONS: Nasal cytology is a tool that provides a more precise differential diagnosis of chronic rhinitis through the study the of nasal mucosa and the identification of "cellular" NAR and OR, even in the pediatric population.

Introduction

The term "rhinitis" is used to indicate the presence of any inflammatory condition of the nasal mucosa. It is defined by the onset of two or more of the following signs and symptoms: nasal congestion, nasal discharge, sneezing, nasal itching, facial pain or pressure, headache, reduction/ loss of smell^{1,2}. With the exception of recurrent infectious rhinitis, chronic rhinitis is a common disease with an incidence of 40% in the Western population³. Through the term "vasomotor" rhinitis, two entities can be defined: allergic rhinitis (AR), in the presence of a relevant aeroallergen sensitization, which is IgE mediated, and non-allergic rhinitis (NAR), whose etiologies, incidence and distribution for sex and age have been less clear so far⁴. Recent studies produced evidence that the hyperreactivity of the nasal mucosa to endogenous and exogenous input is caused by a disorder of the autonomic nervous system. A predominance of the parasympathetic innervation (acetylcholine, VIP) vs. the sympathetic one (norepinephrine, Neuropeptide Y) with vasodilation and nasal gland secretions passing through the vidian nerve fibers, has been observed^{5,6}. When stimulated by noxious agents entering into the nasal cavities, the unmyelinated sensory C-fibers induce the release of several neuropeptides (substance P and neurokinins) and determine nasal itching and sneezing. Over the last years, the diagnosis of non-allergic, non-infectious chronic rhinitis has improved with the introduction of allergic tests made on the skin, nose, and blood and with the dosage of nasal mucosa chemical mediators (eosinophil cationic protein (ECP), tryptase, substance-P)^{7,8}. Moreover, the advent of nasal

Key Words

Chronic rhinitis, Allergy, Nasal cytology, Non-allergic rhinitis, Overlapped rhinitis.

cytology in clinical practice has made it possible to clarify the aspects regarding the physiological or pathological cellular population present in the nasal mucosa and the diagnosis of chronic rhinitis. In fact, based on this assumption, ARIA guidelines better define the group of NAR as "cellular" one⁹. In addition, nasal cytology has been useful for distinguishing a new pathological entity, termed overlapped rhinitis (OR) in which allergic and "cellular" rhinitis co-exist in the same patient¹⁰. Allergic rhinitis is considered a very common condition, affecting about half of the adult population and presenting chronic nasal symptoms^{1,2,11-13}. Various studies have evaluated the incidence of these types of rhinitis: 1.4%-39.7% for the allergic type, between 17% and 50% for NAR, 15-20% for "overlapped" type14-17. However, it is necessary to consider that a lot of these studies did not employ nasal cytology as a diagnostic tool and did not take into consideration the existence of OR. Few studies have been conducted on the pediatric population to define the incidence of NAR. Poddighe et al¹⁸ reported a prevalence of AR with respect to NAR of 3-4:1. Topal et al¹⁹ described an incidence of 76.9% of children with AR. Equally, Chiang et al²⁰ enrolled 660 children, aged 1 to 18 years, and found that 75.9% of them had AR, while the remaining 24.1% had NAR. No data about OR are presented, probably related to the fact that allergen sensitization was rarely performed and that there has been a limited application of nasal cytology in young people until recently²¹. Therefore, the aims of the present study were to evaluate the distribution of chronic rhinopathy in the adult and pediatric populations, to evaluate the cytological features of non-allergic "cellular" rhinitis by classifying it into different subgroups, and to identify OR.

Patients and Methods

This was a retrospective study conducted on 907 patients (461 females, 446 males; average age 40 years, range 4-90 years) with a clinical diagnosis of chronic rhinitis, and enrolled in the Department of Sense Organs of Sapienza University in Rome over the previous two years. Patients were divided into pediatric and adult populations. Hence, we had a group of 135 pediatric patients, 69 females, and 66 males, aged between 4-17 (average age 9.8 years). The adult population was made up of 772 patients, 392 females and 380 males, aged between 18 and 90 years (average age 45.28 years). The inclusion criteria adopted for the study were: presence for 1 year of at least 3 of the following nasal symptoms: nasal obstruction, post-nasal drip, clear rhinorrhea, sneezing, nasal and ocular itching, coughing. The exclusion criteria were: acute infection of the lower airway, deviation of the nasal septum and/or other clinically relevant nasal deformities, local or systemic treatment with corticosteroids, antihistamines, or nasal cromoglycate within the previous 4 weeks. None of the patients received specific immunotherapy for rhinitis.

The study was conducted selecting patients according to a flowchart, based on the ARIA guidelines 2019 (Figure 1)⁹. Patients with a clinical suspicion of rhinitis underwent:

- Nasal endoscopy (2.7 mm 0-degree rigid endoscope).
- Skin Prick test (SPT): a standardized panel inhalant allergens was employed to detect a cutaneous IgE-mediated allergic response in patients, following the criteria imposed by the European Academy of Allergy and Clinical Immunology. The concentration of allergen extracts was 30 HEP (Histamine Equivalent Prick-test; ALK, Milan, Italy). The sensitization was considered when the diameter of the local reaction was equal or greater than 3 mm²²⁻²⁴.
- The dosage of the serum specific IgE was made in all patients with negative SPT.
- CT scan of nasal and sinusal structures (axial, coronal and sagittal projections), in case of suspicion of chronic rhinosinusitis with or without polyposis.
- Nasal cytology: scraping of the nasal mucosa on the middle third of the inferior turbinate was performed by anterior rhinoscopy with the use of a nasal scraping (EP MEDICA Srl, Fusignano, RA, Italy). After sampling, the material was laid on a microscope slide, fixed for air dry, and stained by the May-Grunwald-Giemsa method. The slide was observed under a common light microscope equipped with 1000x objective and supported by a digital camera for the acquisition of the images. The rhinocytogram was obtained reading for fields (not less than 50), in order to observe the cellular elements that composed the normal or pathological nasal mucosa (eosinophils, mast cells, neutrophils, lymphocytes, bacteria, spores, biofilms, and so on)²⁵. The cellular count was made using quantitative and semi-quantitative grading together, as perfect-

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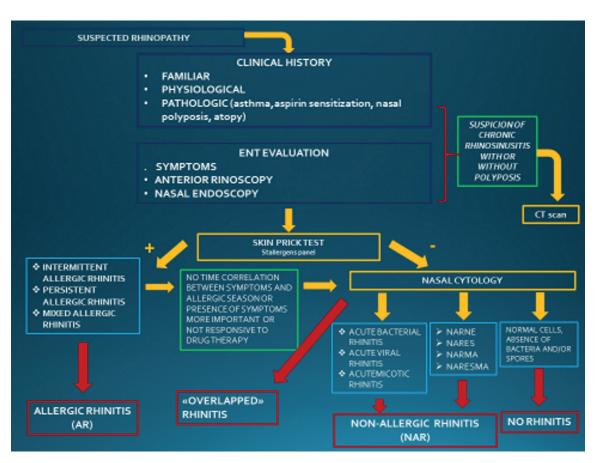


Figure 1. Flow-chart of diagnostic algorithm of chronic rhinitis, based on ARIA criteria 2019.

ed by Meltzer and Jalowayski²⁶. In particular, the bacterial and mycotic counts was defined as grade 0 (not visible), grade 1+ (occasional groups), grade 2+ (moderate number), grade 3+ (easily visible), grade 4+ (elevated number)²⁶ (Table I).

According to the evidence of nasal cytology and of SPT results, the patients were classified as either normal, allergic rhinitis (AR), or non-allergic rhinitis (NAR) patients. Excluding the infective forms of rhinitis, the NAR patients, also defined as cellular rhinitis, were further subdivided into NARNE (neutrophils>50% with absent spores and bacteria); NARES (eosinophils>20%); NARMA (mast cells>10%)²⁷ (Figure 2).

A form of rhinitis, called "overlapped" rhinitis, was detected in a group of the study population, following the Aria 2017 criteria. They presented a more intense nasal symptomatology or were not responsive to medical therapy or failed to present a time correlation between symptomatology and the allergic season²⁸. The SPT and nasal cytology highlighted two possible conditions: a persistent allergic rhinitis in the presence of a rhinocytogram, showing a cell profile different from the typical persistent minimal inflammation, where there are eosinophils>20% and/or mast cells>10%; a coexistence of intermittent allergy and a positive rhinocytogram, eosinophils>20% and / or mast cells>10%, outside the specific pollen season¹⁰.

The Student's *t*-test was performed, and the χ^2 -test and odds ratios were calculated to evaluate the significance of multiple factors within the study groups. A *p*-value of 0.05 was taken as the threshold value for statistical significance.

This study was performed in accordance with the principles of the Declaration of Helsinki and approved by the local Ethics Committee of the University "Sapienza" of Rome.

Results

Regarding the adult population of the study, 471 of 772 patients (61%) presented a clinical-instrumental diagnosis of rhinopathy. Based on the

Description	Quantitative	Grading	Semiquantitative Grading*
Epithelial ciliated	Normal	N/P	Ν
cells	Abnormal	N/P	A (CCP/MN)
Mucinous cells	None	0	0
	Occasional	1-24%	0
	Moderate number	25-29%	2+
	Large number	50-74%	3+
	Covering the entire field	75-100%	4+
Neutrophils and	None	0	0
Eosinophils	Occasional	0.1-1%	1/2+
-	Few scattered cells, small clumps	1.1-5%	1+
	Moderate number, large clumps	5.1-15%	2+
	Large clumps not covering the field	15.1%-20	3+
	Clumps covering entire field	>20%	4+
Basophils	None	0	0
(Mast cells)	Occasional	0.1-0.3%	1/2+
	Few scattered cells, small clumps	0.4-1%	1+
	Moderate number, large clumps	1.1-3%	2+
	Large clumps not covering the field	3.1-6%	3+
	Upt to 25 per an X100 field	>6%	4+
Eosinophil/ Mast cell	None observed	Present/absent	0
degranulation	Occasional granules		1+
-	Moderate number of granules		2+
	Many granules easily seen		3+
	Massive degranulation, entire field		4+
Bacteria and spores	None observed	N/P	0
*	Occasional clumps	N/P	1+
	Moderate number	N/P	2+
	Many cells easily seen	N/P	3+
	Bacteria/spores over the entire field	N/P	4+

Table I. Description and semi-quantitative grading for Nasal Citology reporting.

*CCP: ciliocytophtoria; MN: multinucleation.

results of clinical and physical examinations, and on the Skin prick test and nasal cytology, 213 adult patients (45.2%) with a diagnosis of chronic rhinitis presented AR; 227 patients (48.2%) had NAR; only 31 patients (6.6%) presented OR. Of the total number of patients with AR, 57 (26.7%) had persistent AR, 83 (39%) an intermittent AR, and 73 (34.3%) had a mixed form.

Of the patients with a clinical history, positive for rhinitis and negative for SPT, and submitted to

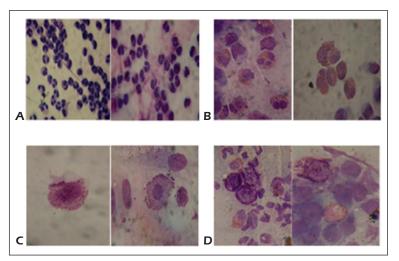


Figure 2. Nasal cytology. A, non-allergic rhinitis with neutrophils (NARNE). B, Non-allergic rhinitis with eosinophils (NARES). C, Non-allergic rhinitis with mast-cells (NAR-MA); non-allergic rhinitis with eosinophils and mast-cells (NARESMA). May-Grunwald-Giemsa staining, magnification x1000.

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N patients (%)	Adult population	Pediatric population	<i>p</i> -value	ODDS RATIO	СІ
TOTAL	772	135			
AR	213 (45.2%)	61 (54.5%)			
AR persistent	57 (26.7%)	26 (42.7%)	0.0023	0.34	0.17-0.7
AR intermittent	83 (39%)	11 (18%)	0.02	2.03	1.13-3.67
AR mixed	73 (34.3%)	24 (39.3%)	0.46	1.24	0.69-2.24
NAR	227 (48.2%)	38 (34%)			
INFECTIOUS	51 (22.5%)	11 (29%)			
CELLULAR	176 (77.5%)	27 (71%)			
NARNE	117 (66.5%)	24 (88.9%)	0.018	4.03	1.17-13.95
NARES	35 (20%)	1 (3.7%)	0.04		
NARMA	10 (5.5%)	1 (3.7%)	0.67		
NARESMA	14 (8 %)	1 (3.7%)	0.43		
OR	31 (6.6%)	13 (11.5%)	0.07	2.05	1.03-4.07
AR+ NARNE	17 (55%)	7 (54%)	0.95	1.04	0.28-3.82
AR+NARES	10 (32.2%)	4 (30.7%)	0.92	1.07	0.26-4.34
AR+ NARMA	3 (9.7%)	2 (15.4%)		0.5	0.09-4.02
AR+ NARESMA	1 (3.1%)	-			
NO RHINITIS	301 (39%)	23 (17.1%)			

Table	ш	Distribution	oft	he subi	ects	with	chronic	rhinitis
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nasal cytology, 22.5% (n= 51) presented an infective cytological pattern, while 77.5% (n=176) presented a pattern of "cellular" NAR. In the "cellular "NAR group, 117 patients (66.5%) were diagnosed as NARNE, 35 (20%) as NARES, 10 (5.5%) as NAR-MA and 14 (8%) as NARESMA. In 6.6% of patients (n=31) nasal cytology made it possible to diagnose a pattern of OR. In particular, 55% presented an overlap of AR and NARNE, 32.2% AR+NARES, 9.7% AR+ NARMA, 3.1% AR+NARESMA (Table II). Regarding age, there was a significant statistical difference between the AR and NAR groups (p=0.004, χ^2 -test), while no differences were found between the other subgroups of rhinopathy (Table III). On the other hand, there were no significant differences in gender between the pathological subgroups within the adult population (Table IV). In the pediatric population of the study (n=135), 112 patients (83%) presented a diagnosis of chronic rhinitis. AR was present in 61 of these 112 patients (54.5%), while 38 patients (34%) had NAR and 13 (11.5%) OR. The division of AR patients, related to the specific aeroallergen sensitization, found that 42.7% of patients had persistent AR (n=26), 39.3% intermittent AR (n= 24), and 18% (n=11) mixed AR. The group of patients with NAR included 29% with infectious rhinitis and 71% with a "cellular" pattern. In particular, in the last group, 24 patients (88.9%) presented nasal cytology with NARNE: of the remaining 3 cases, one (3.7%) had NARES, one (3.7%) NARMA, and one (3.7%) NARESMA. A diagnosis of OR was made in 11.5% of the pediatric population. In particular, 7 cases (54%) were found to have AR+ NARNE, 4 cases (30.7%) AR+NARES, and 2 cases (15.3%) AR+ NARMA (Table II). With regard to age and gender, there were no statistically significant differences between the different subgroups of chronic rhinitis (Table

Table III. Statis	tical evaluation	of rhinitis	distribution	related to	age in a	dult and	pediatric population	1.
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Adult population:age	AR	NAR	OR	
AR	-	<i>p</i> =0.004	<i>p</i> =0.84	
NAR	<i>p</i> =0.004	-	<i>p</i> =0.096	
OR	<i>p</i> =0.84	<i>p</i> =0.096	_	
Pediatric population: age	AR	NAR	OR	
Pediatric population: age	AR _	NAR <i>p</i> =0.11	OR <i>p</i> =0.52	
	AR <i>p</i> =0.11			

ΔΡ	ΝΔΡ	OP	
	INAN	OK	
_	p = 0.74	p = 0.43	
<i>p</i> =0.74	-	p=0.34	
<i>p</i> =0.43	<i>p</i> =0.34	-	
AR	NAR	OR	
_	<i>p</i> =0.10	<i>p</i> =0.98	
0.10		0.20	
p = 0.10	-	p = 0.28	
	<i>p</i> =0.43 AR -	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	- $p=0.74$ $p=0.43$ $p=0.74$ $ p=0.34$ $p=0.43$ $p=0.34$ $-$ AR NAR OR $ p=0.10$ $p=0.98$

Table IV. Statistical evaluation of rhinitis distribution related to gender in adult and pediatric population.

III-Table IV). A more specific statistical analysis based on gender, evidenced a statistically significant correlation between the pediatric and adult populations only within the NARNE subgroup (p=0.0003, γ^2 -test). The results regarding the mean percentage of the predominant cellular type in each subgroup of non-allergic "cellular" rhinitis, for both the adult and pediatric populations, are shown. Considering the presence of one case for the 3 subgroups in the pediatric population, as already described above, in the NARNE subgroups there was not a statistical correlation between the two populations of the study (p=0.84, χ^2 -test). Table IV shows the incidence of the different subgroups of chronic rhinitis, diagnosed with the use of nasal cytology, in adult and pediatric patients. The differences were statistically significant for both intermittent AR (p=0.0023, χ^2 -test; OR 0.34, 95% CI 0.17-0.7) and persistent AR (p=0.02, χ^2 -test; OR 2.03, 95% CI 1.13-3.67), considering that the latter occurred more often in childhood than in adulthood. Therefore, NAR and NARNE occurred more frequently in childhood than in the adult population (p=0.018, χ^2 -test; OR 4.03, 95% CI 1.17-13.95). Indeed, a significant difference was also observed for NARES, considering the more numerous samples in adult patients with respect to the single pediatric case (p=0.04). Additionally, a statistical analysis of the distribution of OR did not reveal any statistically significant differences between the adult and pediatric groups for overlapped rhinitis with NARNE, NARES, and NARMA (respectively p=0.95; p=0.92; p=0.58). It was not possible to match OR with NARESMA due to the paucity of cases in the pediatric population.

Discussion

The diagnosis of rhinitis is generally made taking in consideration the presence of two or more nasal signs and symptoms: nasal congestion, nasal

pressure, headache, reduction/loss of smell^{1,2}. It is extremely important to differentiate between allergic and non-allergic rhinitis to better classify the patient's pathology and so to establish a more precise drug therapy and/or allergen immunotherapy. The diagnosis of AR is established with the evidence of SPT and/or serum allergen-specific IgE, that indicate only the allergen sensitization, in accordance with the patient's clinical signs. When there is no correlation between the symptoms and their temporal onset and allergen exposure, it is assumed that the patient has a form of non-allergic chronic rhinitis, also defined as vasomotor "non-allergic" rhinitis^{4,29-31}. Until now, it has been considered an entity diagnosed on the basis of the exclusion criteria, due to the lack of evidence concerning the incidence and, above all, the effective pathogenesis and the most appropriate definition. Some studies conducted in the allergy clinic centers demonstrated that AR was very common and around 50% of patients with nasal symptomatology had NAR¹¹⁻¹³. Moreover, Mullarkey et al³² found that, of 142 patients, 48% had AR and the remaining 52% had NAR. Differently, two studies, one by Togias et al³³ conducted in 1990 and the other by Moolgard et al³⁴ in 2007, reported an incidence for AR of 83% and 77% and for NAR of 17% and 23%, respectively. A critical evaluation of these studies could be made, considering that the SPT was the only diagnostic tool employed. Currently, the clinical use of nasal cytology has made it possible to formulate a more precise differential diagnosis, not only on the basis of the presence or absence of allergen sensitization, but also on the evaluation of the cellular population in the nasal mucosa and, hence, to better define the classification of chronic rhinitis³⁵. Based on these analyses, the ARIA guidelines introduced the concept of NAR and of "overlapped" rhinitis (presence of mast cells >10% and eosinophil >20%

discharge, sneezing, nasal itching, facial pain or

in the rhynocytogram of patients with persistent allergic rhinitis, differing them from a "minimal persistent inflammation", or in patients with intermittent allergic rhinitis, outside the specific pollen period)^{9,10}. The pathogenetic mechanisms that underlie the onset of NAR and the prevalence of each type of cell in a specific NAR are still unclear. Several studies, especially focused on NARES, demonstrated that the stimulation of the nasal mucosa with irritant agents activates the production of neuropeptides and, consequently, the chemotaxis of T-lymphocytes. The active T-cells, through chemical mediators and interleukins (IL-3, IL-5), locally recall mast-cells and eosinophils which create a self-perpetuating chronic nasal inflammation with a damage of the ciliated epithelium, an increase of nasal permeability to irritant agents, and a nasal hyperreactivity linked to numerous substances and proteins [tryptase, ECP, Mayor Basic Protein (MBP)]⁵⁻⁸.

Over the last years, taking into consideration the application of nasal cytology, only a few epidemiological studies were conducted. Canakcioglu et al³⁶ in 2007 found 48.45% of AR and 51.55% of NAR in a mixed population of pediatric and adult patients. More recently, Gelardi et al³⁷ evidenced 21% of AR and 40% of NAR in a large population of 5030 adult patients. Diversely to the present study, all these authors evaluated the incidence of the different form of chronic rhinitis in a mixed population or in adult patients alone. In this way, the few allergen challenges and the less important chronic, the time-related damage to the nasal mucosa, and the development of complications in childhood are not taken into consideration. Another important aspect was showed by the studies of both Mullarkey et al³² and Gelardi¹⁰ who demonstrated that there is no subdivision in the study population based on the current classification of chronic rhinitis⁹.

To our knowledge, no studies have considered the distribution of the different forms of chronic rhinitis, separately for adults and children.

The results of the present study show that 45.2% of adult patients with a clinical diagnosis of rhinopathy presented AR, 48.2% had NAR, and 6.6% presented an OR. More specifically, patients with AR presented, in relation to the kind of aeroallergen identified with the SPT, persistent disease in 26.7%, an intermittent one in 39%, and mixed rhinitis in 34.3%. Differently, within the NAR group, 66.5% had NARNE, 20% NARES, 8% NARESMA, and a remaining 5.5% had NARMA. On the other hand, Gelardi et al^{38,39}

reported that in adulthood NARESMA and NA-RES were the most frequents forms of NAR, with an incidence of 25-30%. The results obtained could be correlated to the clinical features of the adult population of this study, considering the association of the cellular alterations of the nasal mucosa and the presence of respiratory diseases, such as asthma, sleep-apnea or the exposure to pollutants, chemicals or cigarette smoke⁴⁰.

Regarding the pediatric population, the incidence of rhinitis is still not well-known, because of their less frequent exposure to aeroallergens and/or pollution and the greater difficulties in performing the diagnostic techniques (rhinomanometry, nasal provocation test) for nasal evaluation in children^{4,41,42}. Chiang et al¹⁹ and Topal et al²⁰ studied a population of children with clinical evidence of chronic rhinitis and obtained similar results: 75.9% and 76.9% of AR respectively and, thus, the remaining 24.1% and 23.1% of NAR. In these cases too, the results for NAR were based only on a diagnosis of exclusion. The introduction of nasal cytology into the diagnostic work-up of nasal disorders in the pediatric population, considering its non-invasiveness and painlessness, allowed a more precise estimation of the incidence of NAR and also an identification of OR⁴³. In the present study, all patients were submitted to allergic evaluation. Therefore, it was found that 83% of children presented chronic rhinitis. 54.5% of these had AR (in particular 42.7% with persistent AR), 39.3% with intermittent AR, and 18% with mixed AR. The persistent AR occurred more often in childhood than in the adult group. This data could explain the difference in the results reported by Canakcioglu et al³⁶ who, as already mentioned, found an incidence of 40.52% in mixed groups with persistent AR, 22.33% with intermittent AR, and 37.15% with a mixed form.

NAR was present in 34% of patients with chronic rhinitis and, in particular, 71% of these had a "cellular" nasal disease. More specifically, 88.9% were classified as NARNE and only one case (3.7%) for each of subgroups. Therefore, it was seen that NARNE occurred significantly more often in childhood than in adult age. This is probably attributable to the minor incidence of serious respiratory diseases in children, the minor incidence of polyposis associated with aspirin intolerance and non-allergic asthma, and the higher frequency of fibrous cystic or other ciliary dyskinesia in young adults. Moreover, it is important to consider the exposure to pollutants and/or passive cigarette smoking via parents^{43,44}.

The incidence of OR was estimated by Settipane et al^{15,16} at 34%, while Gelardi et al¹⁰ made an estimate of 15-20%, among all vasomotor rhinopathies. In our study, the nasal cytology made it possible to diagnose a pattern of OR in 6.6% of adult patients (n= 31). In particular, 55% presented an overlap of AR and NARNE, 32.2% AR+NARES, 9.7% AR+NARMA, 3.1% AR+NARESMA. In the pediatric group, a diagnosis of overlapped rhinitis was made in 11.5% of patients, and 54% of them had AR+NARNE. The absence of a statistical difference between pediatric and adult patients could probably be correlated to the small number of cases, above all in the former.

No significant difference was found in the gender distribution for either pediatric or adult patients. Olsson et al⁴⁵ found similar results in their survey regarding a Swedish population with age >19 years. More specifically, a positive statistical result was found between the two populations of the study in the NARNE subgroups of NAR. Settipane et al^{15,16} observed that NAR and OR were more common in female patients than in male ones, independently from age.

As observed by Canakcioglu et al³⁶, the lack of any differences between the cytological evaluations in subgroups of NAR in both study populations could be interpreted considering the possibility of applying the same cytological classification criteria for chronic rhinitis, regardless of age.

Conclusions

We showed that in adults with a clinical diagnosis of rhinopathy, 48.2% of them had NAR, and 6.6% of them had OR. Moreover, in children affected by chronic rhinitis, 34% presented NAR, and 11.5% OR. The introduction of nasal cytology into clinical practice represents an optimal goal considering it as a method to study nasal mucosa, easy to apply even in pediatric patients. It is a tool that provides a more precise differential diagnosis of chronic rhinitis, allowing the identification of "cellular" NAR and "overlapped" rhinitis, and consequently a targeted therapy for each patient.

Conflict of Interests

None of the authors has any conflict of interest, including specific financial interests and relationships.

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