

ORIGINAL ARTICLE

Mixed rhinitis: an underestimated diagnosis in children and adolescents?

Isabella Burla Manhães¹, Fausto Yoshio Matsumoto², Dirceu Solé², Gustavo Falbo Wandalsen²

¹Division of General and Community Pediatrics, Department of Pediatrics, Federal University of São Paulo, São Paulo, Brazil

²Division of Allergy, Clinical Immunology and Rheumatology, Department of Pediatrics, Federal University of São Paulo, São Paulo, Brazil

Summary

Background. Mixed rhinitis (MR) is a potential diagnosis for patients with allergic rhinitis (AR) who present symptoms following exposure to allergens yet also exhibit a significant burden of symptoms after exposure to non-specific irritants. MR is thought to be more prevalent than the isolated form of the disease (AR). However, there are still no established complementary tests or well-defined clinical criteria for diagnosing this phenotype in children and adolescents. This study aimed to propose and evaluate a questionnaire of triggers that could assist in clinically distinguishing patients with MR from those with AR and, through it, to estimate the prevalence of MR in a specialty center. **Methods.** This study focused on patients aged 8 to 18 years diagnosed with AR and under follow-up for at least six months. All patients completed the nasal irritant questionnaire (NIQ) with 18 items. The number of responses with a score ≥ 5 was used to define tertiles. The group from the 3rd tertile onwards was described as "high irritant burden" (MR), while the others were defined as "low irritant burden" (AR). Additionally, symptom control scores, allergic sensitization, atopic comorbidities, and indoor

exposure to aeroallergens were considered. **Results.** By using the diagnostic criterion of MR, defined as at least eight positive responses on the NIQ in a patient with AR, it was possible to determine that the prevalence of MR was 42.9% (54/126), with a predominance of males and adolescents (median 13 years) and a mean duration of 3 years since symptom onset. This group also exhibited poorer symptom control. Considering the other evaluated variables, no significant differences were observed between the groups. **Conclusions.** The prevalence of MR is significant among children with AR, and individuals with MR exhibit poorer symptom control. At least eight positive responses with a score ≥ 5 in the NIQ were a practical cut-off point for differentiating between AR and MR phenotypes.

Key words

Rhinitis; allergic rhinitis; irritants; allergens; child.

Introduction

Rhinitis is an inflammatory nose disorder characterized by symptoms such as nasal congestion, rhinorrhea, sneezing, and itching (1, 2). It is common in children and adolescents and significantly affects their quality of life and overall well-being (3, 4).

Rhinitis is a condition with high heterogeneity, potentially having a variety of subtypes. These subtypes include infectious, allergic (AR), and noninfectious nonallergic (NAR). The condition manifests with considerable variability in the underlying pathophysiological mechanisms (endotypes) and clinical manifestations (phenotypes), making it challenging to develop definitive guidelines for diagnosis and treatment (5).

AR represents the most prevalent form of chronic rhinitis in children and adolescents. The diagnosis is typically based on symptoms triggered by aeroallergens and evidence of allergic sensitization to these allergens (1).

NAR is a chronic condition of the nasal mucosa that predominantly presents with nasal congestion and rhinorrhea without evidence of allergic sensitization (positive immediate hypersensitivity skin test [SPT] and/or specific serum IgE). It is not a single disease with a single underlying cellular mechanism; instead, it is a group of several conditions that cause similar nasal symptoms. These include drug-induced rhinitis, senile rhinitis, hormonal-induced rhinitis, nonallergic occupational rhinitis, gustatory rhinitis, and nonallergic rhinopathy, previously known as vasomotor rhinitis or idiopathic nonallergic rhinitis. The latter is the most prevalent subtype within the NAR group and requires the exclusion of AR as a diagnosis (5).

Mixed rhinitis (MR) is a potential diagnosis for patients with AR who present symptoms following exposure to allergens yet also exhibit a significant burden of symptoms after exposure to nonspecific irritants. This rhinitis phenotype is observed in a substantial proportion of patients with AR and is thought to be more prevalent than the isolated form of the disease (6).

A study of adults with AR, using the IIQ (Irritant Index Questionnaire), revealed that 25% of the subjects were reclassified as having MR. The frequency of symptoms, severity, and occurrence of sinusitis and asthma were all higher in patients with MR than in those who remained diagnosed with AR (7).

The prevalence of NAR in children is unknown; however, a ratio between NAR and AR of at least 1:3 is estimated (8, 9). It is postulated that a proportion of these patients represent the MR subgroup; however, no study has evaluated the pediatric population concerning this diagnosis (10).

This study aimed to describe MR prevalence in children and adolescents treated at a specialized outpatient clinic using an instrument adapted for Brazilian culture (Nasal Irritants Questionnaire, NIQ) and compare demographic and clinical characteristics with those with AR.

Material and methods

This was an analytical cross-sectional study of patients (8 to 18 years old) diagnosed with AR who had been followed up for at least 6 months at the Allergy Outpatient Clinic of the Allergy, Clinical Immunology, and Pediatric Rheumatology Division. The diagnosis of AR was based on the presence of specific nasal symptoms and confirmation of sensitization to at least one allergen, either by serum aeroallergen-specific IgE (UniCap®, ThermoFisher, ≥ 0.35 kU/mL) (11) or by a positive immediate hypersensitivity skin test (SPT; *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Blomia tropicalis*, *Blatella germanica*, *Periplaneta americana*, fungi, dog epithelium, and cat epithelium; IPI Asacpharma®) (12).

Patients were classified according to their clinical presentation (mild intermittent, moderate to severe intermittent, mild persistent, and moderate to severe persistent) (1). The NIQ was completed to ascertain the extent to which primary irritants affect the nasal mucosa, thereby triggering rhinitis symptoms and the effectiveness of symptom control. Patients were classified as monosensitized (i.e., sensitized to a single allergen family) or polysensitized (i.e., sensitized to at least two allergen families).

During the consultation, demographic data and comorbidities were collected, as well as current indoor exposure to dust, animals (dogs, cats, birds), or poor ventilation. Only the presence or absence of each exposure was considered. The Rhinitis Control Assessment Test (RCAT) (13), translated and validated for use in Brazilian culture

(14), and the Visual Analog Scale (VAS) were employed to assess AR symptom control (15, 16).

The NIQ, used to assess exposure to nasal irritants, was developed and adapted for Brazilian culture based on the IIQ (7, 17). The IIQ comprises 20 items, with a numerical gradation from 0 to 10, where 10 corresponds to the worst possible scenario. In summary, the initial new questionnaire incorporated some common irritants (makeup, hair dye, nail polish, fake nail glue, deodorant, fabric softener, and electronic cigarette smoke).

This questionnaire (27 items) was administered to a pilot group, and irritants with low scores (less than 20% positive responses; scores ≥ 5) were excluded. Subsequently, the items were regrouped, and the final nasal irritant questionnaire (NIQ) was constructed (Figure 1), which comprised 18 items. By the evaluation criteria, a score ≥ 5 for each question was deemed clinically relevant. The number of questions with clinically relevant answers was divided into tertiles. The division into tertiles was arbitrary, aiming to differentiate between two well-defined groups (high burden of irritants vs. low burden of irritants). The first two tertiles indicated a low burden of irritants, while the last tertile ($\geq$ eight items with a score of ≥ 5 in NIQ) indicated a high burden of irritants, with these patients being diagnosed with MR. Consequently, this study proposes a novel definition for diagnosing MR, characterized by the concurrence of allergic rhinitis and a high burden of irritants in the same patient.

(Figure 1 - Nasal Irritants Questionnaire – NIQ.)

Parametric and non-parametric tests were employed considering the characteristics of the variables under investigation. The rejection level for the null hypothesis was set at 5%.

Results

The study included 126 participants (65.9% male) with a median age of 13 (8 to 18). All subjects had moderate to severe persistent rhinitis. Regarding other atopic conditions, 75.4% of the participants had asthma, 71.4% had atopic dermatitis, and 50% had ocular allergies. Descriptive data on the study population are presented in

Table I.

(Table I)

Table II illustrates the frequency of positive responses to the items of the NIQ. The results demonstrate that temperature change (95.2%), mold or mildew odor (85.7%), high air pollution (84.9%), tobacco smoke (81%), and cold air (81%) were the most frequently identified triggers. The least commonly considered irritant was cosmetics/makeup, with 19.8% of positive responses. Considering a score ≥ 5 for each item, temperature change remained the most relevant (80.2%) and cosmetics/makeup the least (7.1%).

(Table II)

We have found a median of 11 (interquartile range 7-14) positive answers to the questions of the NIQ. When only the items with a score ≥ 5 were considered, the

median was 6 (interquartile range 3–10) (**Table IIIa**). **Table IIIa** shows the study group's answers to the questions on nasal irritants. These analyses showed that the cut-off point effectively discriminated between MR and AR.

Patients were classified according to the number of positive answers distributed in tertiles into two groups: those with a high burden of irritants (from the third tertile onwards; 54 or 42.9%) and those with a low burden of irritants (below the third tertile; 72 or 57.1%) (**Table IIIb**).

(Table IIIa and IIIb)

A significant difference ($p < 0.001$) was observed between the MR and AR groups regarding the symptom control scores. Patients with MR exhibited worse symptom control, as evidenced by lower RCAT scores and higher VAS scores (**Table IV**).

(Table IV)

There was no significant association between exposure to aeroallergens in the home environment—house dust ($p = 0.380$), dogs ($p = 0.351$), cats ($p = 0.228$)—or sensitization patterns and the MR diagnosis. The data indicate that both groups were primarily sensitized to *Dermatophagoides pteronyssinus*, with a dominant monosensitization pattern observed (62.7%), and there was no significant difference between the MR and AR groups ($p = 0.288$). Regarding the treatment regimen, most patients were on monotherapy, with continuous topical nasal corticosteroids and oral

antihistamines when needed (79.4% of the total sample, 77.8% MR, and 80.5% AR). No statistically significant difference was observed regarding the type of treatment administered between the two groups ($p = 0.703$). The most frequent rhinitis-related diseases were asthma (75.4%) and atopic dermatitis (71.4%), with no differences according to rhinitis phenotype.

Discussion

It is established that 60% of patients with AR present symptoms when exposed to irritating substances, probably by nonallergic mechanisms (18). The simultaneous presence of underlying AR and nonallergic rhinopathy mechanisms is a defining feature of MR. There are no established complementary tests or well-defined clinical criteria for diagnosing MR. All clinical assessment instruments inquire about nasal symptoms but do not address the potential triggers. Patients with MR present symptoms when exposed to a wide variety of substances, which presents a challenge to disease management (10, 19). Another point of interest is the ongoing debate about the optimal terminology for the condition. Specifically, there has been discussion regarding whether "AR with high burden" or "mixed rhinitis" is the more suitable term (7). In this author's opinion, both terms refer to the same disease. However, it is essential to retain the MR terminology. This is important because it enables the condition to be described as a unique phenotype, distinct from both AR and NAR, thus avoiding misunderstandings. In light of the abovementioned knowledge, it became evident that developing a specific instrument for assessing MR in the pediatric age was necessary.

The NIQ was an effective auxiliary diagnostic tool for MR in this population. The third tertile of the responses with a score of at least five was used as the cut-off to discriminate between the groups regarding the intensity of response to nasal irritants. The diagnosis of MR was made when an individual belonged to this group and had proven allergic sensitization. The prevalence of MR in our sample was 42.9%, comparable to the prevalence observed in adults (7). In patients without allergic sensitization, a high burden of irritants can indicate the diagnosis of nonallergic rhinopathy.

In the population assessed by the original IIQ, a 47% prevalence of MR was observed among those previously diagnosed with AR (7), which is consistent with our findings. Additionally, this study indicated that patients with MR exhibited worse scores on the IIQ (7). To our knowledge, no study has yet evaluated the prevalence of nasal symptoms triggered by primary irritants in children and adolescents with aeroallergen sensitization.

The results of our study revealed a statistically significant difference in the total VAS score and the scores for each of the individual symptoms, with the patients with MR exhibiting higher scores on all of them. All patients were classified as having moderate to severe persistent rhinitis; however, none were diagnosed with NAR.

The visual analog scale (VAS) has been validated for quantifying symptoms in various contexts for children aged 6 and older, adolescents, and adults (5). It has been widely used to assess the severity of rhinitis (21-23). The RCAT (Rhinitis Control Assessment Test) is also employed in clinical practice to assess rhinitis symptoms control and evaluate treatment response (14, 24).

The scores and classification provided by the RCAT were also worse in patients with MR than those with AR. The data observed by other authors indicate that pediatric

patients with AR exhibit worse symptom control compared to those with NAR, yet no mention is made of MR (8, 9). In adults, MR diagnosis was associated with current symptoms and persistent rhinitis (65% MR vs 45% AR, $p<0.01$) (25).

Sensitization pattern and etiological agent exhibited no discernible differences between the two groups under evaluation and reported by others (7-9).

Upon evaluating the treatment received by patients with AR and those with MR, Chiang et al. observed that the latter group utilized antileukotrienes with greater frequency. At the same time, the former exhibited a higher rate of inhaled corticosteroid prescriptions, suggesting a potential correlation with asthma (8). The use of oral antihistamines and topical nasal corticosteroids did not differ between the groups (8). In our study, 77.8% of patients with MR and 80.5% of those with AR utilized only nasal topical corticosteroids and oral antihistamines when needed ($p=0.703$).

Another point assessed by the researchers is the presence of allergic comorbidities in patients with MR. A study of adults with MR showed a significantly higher prevalence of asthma among those with MR compared to those with AR (31% vs. 21%, $p<0.01$) (7). No significant differences were observed between the MR and AR groups in our study population.

The available data on MR in adults indicates a higher mean age in relation to those with AR and a predominance of females (7). The present study compared children with AR versus MR and found no significant differences in age, length of illness, or gender.

One of the study's limitations was the relatively small number of patients evaluated and the exclusive inclusion of AR patients, which may not fully align with the characteristics of the general population. A notable observation is the lack of seasonal rhinitis cases within the studied population. This observation underscores the need to

implement the NIQ in other countries where this disease is common. Doing so would enable us to validate the questionnaire's effectiveness in helping diagnose mixed rhinitis in patients with seasonal rhinitis.

In conclusion, MR prevalence was high among children and adolescents with AR. MR was associated with poorer control and more severe nasal symptoms than AR. The NIQ was an effective method for differentiating between AR and MR groups. At least eight questions with a positive answer and a score of 5 or more proved to be a practical cut-off point for differentiating these phenotypes. Further research is required to increase knowledge about MR, especially in children, to develop a more accurate diagnostic and therapeutic approach to the disease, which will contribute to improving patients' quality of life.

Declaration of conflicting interest: The authors declare that they have no competing interests with respect to the research, authorship, and/or publication of this article.

Funding statement: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Contributions:

IBM: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing - original draft.

FYM: Validation, Visualization, Writing - original draft and Writing - review & editing.

GFM: Conceptualization, Data curation, Investigation, Supervision, Validation, Visualization, Writing - original draft and Writing - review & editing.

DS: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Validation, Visualization, Writing - original draft and Writing - review & editing.

Acknowledgements:

Statements and declarations: The study was approved by the Human Research Ethics Committee of the Federal University of São Paulo under protocol number 5.724.378 (CAAE 62443822.9.0000.5505). Respondents gave written consent for review and signature before starting interviews.

References

- 1 Bousquet J, Van Cauwenberge P, Khaltaev N, Aria Workshop Group, World Health Organization. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol.* 2001;108(5 Suppl):S147-334. doi: 10.1067/mai.2001.118891.
- 2 Roberts G, Xatzipsalti M, Borrego LM, et al. Paediatric rhinitis: position paper of the European Academy of Allergy and Clinical Immunology. *Allergy.* 2013;68(9): 1102–16. doi: 10.1111/all.12235.
- 3 Bachert C. Persistent rhinitis - allergic or nonallergic? *Allergy.* 2004;59(Suppl 76): 11–5. doi: 10.1111/j.0108-1675.2004.00389.x.
- 4 Tran NP, Vickery J, Blaiss MS. Management of Rhinitis: Allergic and Non-Allergic. *Allergy Asthma Immunol Res.* 2011; 3(3):148-56. doi: 10.4168/aair.2011.3.3.148.

- 5 Papadopoulos NG, Guibas GV. Rhinitis Subtypes, Endotypes, and Definitions. *Immunol Allergy Clin North Am.* 2016;36(2):215-33. doi: 10.1016/j.iac.2015.12.001.
- 6 Settipane RA, Kaliner MA. Nonallergic rhinitis. *Am J Rhinol Allergy.* 2013;27(Suppl 1):S48-51. doi: 10.2500/ajra.2013.27.3927.
- 7 Bernstein JA, Levin LS, Al-Shuik E, et al. Clinical characteristics of chronic Rhinitis patients with high vs low irritant trigger burdens. *Ann Allergy Asthma Immunol.* 2012;109(3):173-8. doi: 10.1016/j.anai.2012.06.013.
- 8 Chiang WC, Chen YM, Tan HKK, et al. Allergic rhinitis and non-allergic rhinitis in children in the tropics: prevalence and risk associations. *Pediatr Pulmonol.* 2012;47(10):1026-33. doi: 10.1002/ppul.22554.
- 9 Topal E, Bakirtas A, Yilmaz O, et al. Predictive factors to differentiate between allergic and nonallergic rhinitis in children. *Int Forum Allergy Rhinol.* 2014;4(6):447-52. doi: 10.1002/alr.21312.
10. Poddighe D, Gelardi M, Licari A, et al. Non-allergic rhinitis in children: Epidemiological aspects, pathological features, diagnostic methodology and clinical management. *World J Methodol.* 2016;6(4):200-213. doi: 10.5662/wjm.v6.i4.200.
- 11 Sacco C, Perna S, Vicari D, et al. Growth curves of 'normal' serum total IgE levels throughout childhood: A quantile analysis in a birth cohort. *Pediatr Allergy Immunol.* 2017;28(6):525-534. doi: 10.1111/pai.12738.
- 12 Hong SD, Ryu G, Seo MY, et al. Optimal cutoff values of allergen-specific immunoglobulin E to house dust mites and animal dander based on skin-prick test results: Analysis in 16,209 patients with allergic rhinitis. *Am J Rhinol Allergy.* 2018;32(1):23-26. doi: 10.2500/ajra.2018.32.4483.

- 13 Meltzer EO, Schatz M, Nathan R, et al. Reliability, validity, and responsiveness of the Rhinitis Control Assessment Test in patients with rhinitis. *J Allergy Clin Immunol*. 2013;131(2):379-86. doi: 10.1016/j.jaci.2012.10.022.
- 14 Fernandes PH, Matsumoto F, Solé D, et al. Translation into Portuguese and validation of the Rhinitis Control Assessment Test (RCAT) questionnaire. *Braz J Otorhinolaryngol*. 2016;82(6):674-679. doi: 10.1016/j.bjorl.2015.12.011.
- 15 Klimek L, Bergmann K-C, Biedermann T, et al. Visual analogue scales (VAS): Measuring instruments for the documentation of symptoms and therapy monitoring in cases of allergic rhinitis in everyday health care: Position Paper of the German Society of Allergology (AeDA) and the German Society of Allergy and Clinical Immunology (DGAKI), ENT Section, in collaboration with the working group on Clinical Immunology, Allergology and Environmental Medicine of the German Society of Otorhinolaryngology, Head and Neck Surgery (DGHNOKHC). *Allergo J Int*. 2017;26(1):16-24. doi: 10.1007/s40629-016-0006-7.
- 16 Bousquet J, Schünemann HJ, Hellings PW, et al. MACVIA clinical decision algorithm in adolescents and adults with allergic rhinitis. *J Allergy Clin Immunol*. 2016;138(2):367-374.e2. doi: 10.1016/j.jaci.2016.03.025.
- 17 Brandt D, Bernstein JA. Questionnaire evaluation and risk factor identification for nonallergic vasomotor rhinitis. *Ann Allergy Asthma Immunol*. 2006;96(4):526-32. doi: 10.1016/S1081-1206(10)63546-6.
- 18 Scarupa MD, Kaliner MA. Nonallergic rhinitis, with a focus on vasomotor rhinitis: clinical importance, differential diagnosis, and effective treatment recommendations. *World Allergy Organ J*. 2009;2(3):20-5. doi: 10.1097/WOX.0b013e3181990aac.

- 19 Greiwe JC, Bernstein JA. Allergic and Mixed Rhinitis: Diagnosis and Natural Evolution. *J Clin Med*. 2019;8(11):2019. doi: 10.3390/jcm8112019.
- 20 Bousquet PJ, Combescure C, Neukirch F, et al. Original article: Visual analog scales can assess the severity of rhinitis graded according to ARIA guidelines. *Allergy*. 2007;62(4):367-72. doi: 10.1111/j.1398-9995.2006.01276.x.
- 21 Solé D, Kuschnir FC, Pastorino AC, et al. V Brazilian Consensus on Rhinitis – 2024. *Braz J Otorhinolaryngol*. 2024;91(1):101500. doi: 10.1016/j.bjorl.2024.101500.
- 22 Spector SL, Nicklas RA, Chapman JA, et al. Symptom severity assessment of allergic rhinitis: part 1. *Ann Allergy Asthma Immunol*. 2003;91(2):105-14. doi: 10.1016/s1081-1206(10)62160-6.4.
- 23 Demoly P, Bousquet PJ, Mesbah K, et al. Visual analogue scale in patients treated for allergic rhinitis: an observational prospective study in primary care: Asthma and Rhinitis. *Clin Exp Allergy*. 2013;43(8):881-8. doi: 10.1111/cea.12121.
- 24 Nathan RA, Dalal AA, Stanford RH, et al. Qualitative Development of the Rhinitis Control Assessment Test (RCAT), an Instrument for Evaluating Rhinitis Symptom Control. *Patient*. 2010;3(2):91-9. doi: 10.2165/11318410-000000000-00000.
- 25 D'Elia C, Gozal D, Bruni O, et al. Allergic rhinitis and sleep disorders in children – coexistence and reciprocal interactions. *J Pediatr (Rio J)*. 2022;98(5):444-454. doi: 10.1016/j.jped.2021.11.010.

Table Ia. Characteristics of participants

Characteristics	Total sample N=126
Sex^a	
- Male	83 (65.9)
Age (years)^b	13 (10-15)
Age of onset of symptoms (years)^b	3 (1-5)
Length of illness (years)^b	9 (7-12)
Comorbidities^a	
- Asthma	95 (75.4)
- Eye allergy	63 (50)
- Atopic dermatitis	90 (71.4)
- Food allergy	6 (4.8)
Indoor exposure to allergens^a	
- Dust	69 (54.8)
- Dog	55 (43.7)
- Cat	17 (13.5)
- Bird	22 (17.5)
- Humidity	17 (13.5)
Sensitization^a	
- House dust mites	126 (100)
- Epithelium	45 (35.7)
- Fungi	16 (12.7)
Sensitization pattern^a	
- Monosensitized	79 (62.7)
RCAT score^c	21 (4)

^a Categorical variables presented as the total number of patients and percentage

^b Continuous variables with asymmetric distribution presented as the median and interquartile range

^c Continuous variables with normal distribution presented as mean and standard deviation

Table Ib. Characteristics of the Allergic rhinitis and Mixed Rhinitis subgroups.

	Mixed rhinitis n=54	Allergic rhinitis n=72	P
Male sex ^a	31 (57.4)	52 (72.2)	0.083
Age (years) ^b	13 (10-15)	13 (11-15)	0.829
Age of onset (years) ^b	3 (1-5)	3 (1-5)	0.831
Length of illness (years) ^c	9 (3)	9 (4)	0.647

^a Categorical variables presented as absolute values and percentages; Chi-square test

^b Continuous variables with asymmetric distribution presented as median and interquartile range; Mann-Whitney test.

^c Continuous variables with normal distribution presented as mean and standard deviation; Student's t-test

Table II. Questions answers to final nasal irritants questionnaire (NIQ) version

Questions	Positive responses (%)	Answers with a score ≥ 5 (%)
1) Temperature change	95.2	80.2
2) Wall paint or varnish	73.8	46.0
3) Mold or mildew odor	85.7	61.9
4) Tobacco smoke	81.0	58.7
5) Electronic cigarette smoke	42.9	24.6
6) Sawdust	65.1	38.1
7) High air pollution	84.9	58.7
8) Cold air, cold wind, air conditioning	81.0	61.1
9) Perfume	71.4	47.6
10) Solvents or acetone	50.0	26.2
11) Bleach or chlorine	62.7	40.5
12) Household cleaners	54.0	27.8
13) Disinfectants	49.2	27.8
14) Ammonia (hair dye)	38.1	19.8
15) Cosmetics or makeup	19.8	7.1
16) Fabric softener	42.9	22.2
17) Soap powder	35.7	13.5
18) Deodorant	39.7	23.0

Table IIIa. Group effect on total score, positive responses and clinically relevant answers to the NIQ

	Total sample	Mixed rhinitis N = 54	Allergic rhinitis N = 72	p
Complete questionnaire				
- Total score (median, interquartile range)	57 (31-86)	92 (76-111)	33 (24-49)	<0.001
- N°. of positive responses	11 (7-14)	14 (13-16)	7 (6-10)	<0.001
- N°. of answers ≥ 5*	6 (3-10)	11 (8-13)	4 (2-5)	<0.001
Question 1 - Temperature change				
- Total score	795	415	380	<0.001
- Median total score	6	8	5	-
- N°. of positive responses	120	54	66	0.031
- N°. of answers ≥ 5*	101	53	48	<0.001
Question 2 – Paints or varnish				
- Total score	540	373	167	<0.001
- Median total score	4	8	1	-
- N°. of positive responses	93	51	42	<0.001
- N°. of answers ≥ 5*	58	43	15	<0.001
Question 3 - Mold or mildew odors				
- Total score	728	404	324	<0.001
- Median total score	6	9	4	-
- N°. of positive responses	108	49	59	0.166
- N°. of answers ≥ 5*	78	44	34	<0.001
Question 4 - Tobacco smoke				
- Total score	655	392	263	<0.001
- Median total score	5	8	3	-
- N°. of positive responses	102	49	53	0.016
- N°. of answers ≥ 5*	74	47	27	<0.001
Question 5 – Electronic cigarette smoke				
- Total score	301	201	100	<0.001
- Median total score	0	2	0	-
- N°. of positive responses	54	31	23	0.004
- N°. of answers ≥ 5*	31	23	8	<0.001
Question 6 – Sawdust				
- Total score	458	311	147	<0.001
- Median total score	3	6	1	-
- N°. of positive responses	82	45	37	<0.001
- N°. of answers ≥ 5*	48	34	14	<0.001
Question 7 - High air pollution				
- Total score	691	426	265	<0.001
- Median total score	6	9	3	-
- N°. of positive responses	107	53	54	<0.001
- N°. of answers ≥ 5*	74	48	26	<0.001
Question 8 - Cold air, cold wind, air conditioning				
- Total score	632	386	246	<0.001
- Median total score	5	7	4	-
- N°. of positive responses	102	53	49	<0.001
- N°. of answers ≥ 5*	77	47	30	<0.001
Question 9 - Perfumes				
- Total score	535	359	176	<0.001
- Median total score	3	8	1	-
- N°. of positive responses	90	50	40	<0.001
- N°. of answers ≥ 5*	60	43	17	<0.001
Question 10 - Solvent or acetone				
- Total score	311	243	68	<0.001
- Median total score	0	5	0	-
- N°. of positive responses	63	41	22	<0.001
- N°. of answers ≥ 5*	33	28	5	<0.001
Question 11 – Bleach or chlorine				
- Total score	470	342	128	<0.001
- Median total score	3	6	0	-
- N°. of positive responses	79	48	31	<0.001
- N°. of answers ≥ 5*	51	39	12	<0.001
Question 12 – Household cleaners				

- Total score	350	286	64	<0.001
- Median total score	1	6	0	-
- N°. of positive responses	68	46	22	<0.001
- N°. of answers $\geq 5^*$	35	31	4	<0.001
Question 13 - Disinfectants				
- Total score	328	260	68	<0.001
- Median total score	0	5	0	-
- N°. of positive responses	62	43	19	<0.001
- N°. of answers $\geq 5^*$	35	28	7	<0.001
Question 14 - Ammonia (hair dye)				
- Total score	239	183	56	<0.001
- Median total score	0	3	0	-
- N°. of positive responses	48	32	16	<0.001
- N°. of answers $\geq 5^*$	25	20	5	<0.001
Question 15 - Cosmetics and makeup				
- Total score	93	77	16	0.008
- Median total score	0	0	0	-
- N°. of positive responses	25	16	9	0.018
- N°. of answers $\geq 5^*$	9	9	0	<0.001
Question 16 - Fabric softener				
- Total score	261	225	36	<0.001
- Median total score	0	4	0	-
- N°. of positive responses	54	37	17	<0.001
- N°. of answers $\geq 5^*$	28	27	1	<0.001
Question 17 - Soap powder				
- Total score	188	151	37	<0.001
- Median total score	0	2	0	-
- N°. of positive responses	45	29	16	<0.001
- N°. of answers $\geq 5^*$	17	15	2	<0.001
Question 18 - Deodorant				
- Total score	253	204	49	<0.001
- Median total score	0	3	3	-
- N°. of positive responses	50	36	14	<0.001
- N°. of answers $\geq 5^*$	29	24	5	<0.001

Continuous variables with asymmetric distribution, presented in absolute value (count); Mann-Whitney test

* a score ≥ 5 for each question was deemed clinically relevant

Table IIIb. Division of groups based on tertiles

Tertiles	N	Percentages	Group	Diagnosis
First	35	27.8	Low Irritant burden	Allergic Rhinitis
Second	37	29.4	Low Irritant burden	Allergic Rhinitis
Third	54	42.9	High irritant burden	Mixed Rhinitis

Table IV. Comparisons of RCAT (Rhinitis Control Assessment Test) and VAS (Visual Analog Scale) between children with mixed rhinitis (MR) and allergic (AR).).

	Mixed rhinitis n=54	Allergic rhinitis n=72	P
RCAT score ^a	19 (16-22)	22 (19-25)	<0.001
VAS sneezing ^a	2.5 (1.1-4.7)	0.5 (0-1.9)	<0.001
VAS rhinorhea ^a	3.1 (0.5-6)	0.5 (0-3.7)	0.002
VAS nasal obstruction ^a	2.4 (0-5.5)	0.2 (0-2.1)	0.003
VAS itching ^a	1.5 (0.3-4.5)	0.3 (0-1.5)	0.002
Total VAS ^a	4 (0.7-6.0)	1.8 (0.3-4.6)	0.014
RCAT classification ^b			0.007
- Controlled	17 (31.5)	40 (55.6)*	
- Uncontrolled	37 (68.5)	32 (44.4)	
VAS classification ^b			0.008
- Controlled	15 (27.8)	39 (54.2)*	
- Partially controlled	17 (31.5)	18 (25.0)	
- Uncontrolled	22 (40.7)	15 (20.8)	

^a Continuous variables with asymmetric distribution presented as median and interquartile range; Mann-Whitney test

^b Categorical variables presented as absolute values and percentages; Chi-square test

* Group responsible for significance

Do you sneeze, or does your nose itch, run, or stuff up when you come into contact with the substances below?

Instructions: Please rate on a scale of 0 to 10 the degree to which the following irritants cause or aggravate your symptoms. "0" means that the substance does not trigger or worsen any symptoms, and "10" means that the substance triggers unbearable symptoms (the worst possible).



0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----



1) Temperature changes?	0	1	2	3	4	5	6	7	8	9	10
2) Paints or varnish?	0	1	2	3	4	5	6	7	8	9	10
3) Mold or mildew odors?	0	1	2	3	4	5	6	7	8	9	10
4) Tobacco smoke?	0	1	2	3	4	5	6	7	8	9	10
5) Electronic cigarette smoke?	0	1	2	3	4	5	6	7	8	9	10
6) Sawdust?	0	1	2	3	4	5	6	7	8	9	10
7) Periods of high air pollution?	0	1	2	3	4	5	6	7	8	9	10
8) Cold air, cold wind, or air conditioning?	0	1	2	3	4	5	6	7	8	9	10
9) Perfumes?	0	1	2	3	4	5	6	7	8	9	10
10) Solvents or acetone?	0	1	2	3	4	5	6	7	8	9	10
11) Bleach or chlorine?	0	1	2	3	4	5	6	7	8	9	10
12) Household cleaners?	0	1	2	3	4	5	6	7	8	9	10
13) Disinfectants?	0	1	2	3	4	5	6	7	8	9	10
14) Ammonia (hair dye)?	0	1	2	3	4	5	6	7	8	9	10
15) Cosmetics or makeup?	0	1	2	3	4	5	6	7	8	9	10
16) Fabric softener?	0	1	2	3	4	5	6	7	8	9	10
17) Soap powder?	0	1	2	3	4	5	6	7	8	9	10
18) Deodorant?	0	1	2	3	4	5	6	7	8	9	10

At least 8 questions with a positive answer (score ≥ 5) = **HIGH IRRITANT BURDEN**
 Less than 8 questions with a positive answer (score ≥ 5) = **LOW IRRITANT BURDEN**