



Influence of nasal septum deformity on nasal obstruction, disease severity, and medical treatment response among children and adolescents with persistent allergic rhinitis



Franklin Mariño-Sánchez ^{a, b, c, *, 1}, Meritxell Valls-Mateus ^{c, d},
Paulina Cardenas-Escalante ^a, Oliver Haag ^a, Karen Ruiz-Echevarría ^e,
Rosa Jiménez-Feijoo ^e, Jaime Lozano-Blasco ^e, María T. Giner-Muñoz ^e,
Ana M. Plaza-Martin ^e, Joaquim Mullol ^{c, d, **}

^a Servicio de Otorrinolaringología, Hospital Sant Joan de Déu, Barcelona, Spain

^b Unidad de Rinología, Servicio de Otorrinolaringología, Hospital Universitario Ramón y Cajal, Madrid, Spain

^c Immunoal·lèrgia Respiratòria Clínica i Experimental (IRCE), Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), CIBERES, Barcelona, Catalonia, Spain

^d Unitat de Rinologia i Clínica de l'Olfacte, Servei d'Otorrinolaringologia, Hospital Clínic, Barcelona, Catalonia, Spain

^e Secció de Imunoal·lèrgia, Servei de Pediatria, Hospital Sant Joan de Déu, Barcelona, Spain

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ABSTRACT

Objective: To evaluate the impact of different types of nasal septum deformity (NSD) on nasal obstruction, rhinitis severity and response to medical treatment among pediatric persistent allergic rhinitis (PER) patients.

Methods: In a prospective, real-life study, 150 children and adolescents (mean age 13 ± 2.8 years, females 32.6%) diagnosed with PER according to ARIA guidelines were assessed by nasal endoscopy for NSD according to Mladina's classification, their response to medical treatment (intranasal steroids and antihistamines or antileucotriens), the presence of comorbidities, rhinitis severity (modified-ARIA criterion) and nasal obstruction visual analog scale score (VAS).

Results: Most patients (87%) had 1 of the 7 types of septal deformities. There was a high prevalence of bilateral (types 4 and 6; 46%) and anterior unilateral (types 1 and 2; 25%) NSD in patients not responding to medical treatment. Type 4 (OR = 6.4; $p = 0.005$) or type 6 (OR = 4.4; $p = 0.03$) NSD increased the risk of lack of improvement with medical treatment. Coexistence of anterior unilateral or bilateral NSD with severe turbinate enlargement increased >20-fold the risk of lack of improvement. Patients with bilateral NSD presented greater rhinitis severity. Non-responder adolescents displayed higher prevalence of bilateral NSD than children (53% vs. 23%; $p = 0.02$). Nasal obstruction VAS was higher for patients with anterior than posterior NSD, and greater for patients with bilateral NSD than any other type of septal morphology.

Conclusion: Nasal endoscopy shows that bilateral and unilateral anterior nasal septum deformities are strongly associated with a poor response to medical treatment, greater rhinitis severity and higher nasal obstruction VAS. Consequently, nasal endoscopy is necessary in the PER patients to understand the disease severity as well as to plan a specific surgical treatment in order to improve nasal obstruction, disease severity, and patient's quality of life.

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* Corresponding author. Servicio de Otorrinolaringología, Hospital Sant Joan de Déu, Passeig de Sant Joan de Déu 2, 08950 Esplugues de Llobregat, Barcelona, Spain.

** Corresponding author. Unitat de Rinologia i Clínica de l'Olfacte, Servei d'Otorrinolaringologia, Hospital Clínic, Barcelona, Catalonia, Spain.

E-mail addresses: franklinmarino@gmail.com (F. Mariño-Sánchez), jmullol@clinic.cat (J. Mullol).

¹ Present address: Unidad de Rinología, Servicio de Otorrinolaringología, Hospital Universitario Ramón y Cajal, Ctra. de Colmenar Viejo km. 9,100, 28034 Madrid, Spain.

1. Introduction

Nasal septal deformity (NSD) is one of the most common anatomic disorders in humans. Up to 48% of children and adolescents in the general population present NSD [1]. However, prevalence varies among different studies due to the lack of a standardized method with a detailed morphologic systematization for describing particular NSD. There are a variety of NSD requiring specific management to achieve predictable results [2]. In this regard, Mladina et al. developed a simple classification in 7 types of NSD, which has been validated in children from different geographic regions [3].

In the NODPAR study [4], we previously demonstrated that nasal obstructive disorders such as turbinate enlargement (TE) and septal deviation, but not adenoidal hyperplasia, are strongly associated with the presence of severe rhinitis, worse nasal symptoms scores, and poor response to medical treatment in pediatric persistent allergic rhinitis (PER) patients. However, “septal deviation” is a generic term that do not sufficiently define septum abnormalities. There are a variety of septal deformities that may affect the quality of nasal breathing in different ways [5], and would require specific management among PER patients to accomplish predictable results.

To our knowledge there are no published studies describing nasal septum morphology among pediatric allergic rhinitis patients nor its relationship with medical treatment failure or rhinitis severity.

The principal aim of this study was to evaluate, using Mladina's classification, the impact of different types of NSD on nasal obstruction, rhinitis severity, and response to medical treatment among pediatric PER patients.

2. Methods

2.1. Study population and design

This was a real-life, non-randomized, prospective, open-label study performed from February 2014 to March 2016. Children and adolescents ($n = 150$) diagnosed with PER according to ARIA guidelines criteria (nasal symptoms for more than 4 days a week and for more than 4 consecutive weeks) [6], referred from Allergy to ENT Department at Sant Joan de Déu Children's Hospital were included. All patients received treatment with daily oral intranasal steroids (fluticasone or mometasone) for at least 2 consecutive months at recommended doses. Non-asthmatic subjects added daily antihistamines (desloratadine). Asthmatic patients received daily leukotriene receptor antagonists (montelukast).

PER severity was assessed by the m-ARIA items [7] (sleep, daily activities/sport/leisure, school performance, and troublesome symptoms) to classify pediatric patients on three different levels: mild (no items affected), moderate (1–3 items affected) and severe (all of four items affected).

After treatment adherence was corroborated by direct questioning (forgetfulness of using intranasal steroids less than 8 times in 2 months), patients were asked by a previously validated question [4]: “Have your symptoms of allergic rhinitis improved with the treatment? (yes or no)”. Patients with lack of improvement of nasal symptoms ($n = 100$) were included in the non-responder (NR) group, while patients with successful improvement after medical treatment ($n = 50$) were included in the responder (R) group.

Patients were scheduled for septoplasty (minimally aggressive if they were <12 years old) and/or turbinoplasty, and/or adenoidectomy, depending on endoscopic findings; septal deformity, severe turbinate enlargement and adenoidal hyperplasia, respectively.

Demographic data (age and gender) and the presence of comorbidities including asthma, conjunctivitis, and chronic

rhinosinusitis (CRS) according to EPOS criterion [9] were evaluated. According to age, patients were stratified in two groups for analysis: children (6–11 years) and adolescents (12–17 years).

Exclusion criteria were: upper respiratory tract infection in the last two weeks, known psychiatric or neurocognitive impairment, previous nasal surgery, or the presence of a serious concomitant illness.

The Ethics Committee of our institution approved the study and signed informed consent was obtained from patient's legal guardians.

2.2. Outcomes

2.2.1. Nasal obstruction symptom

A visual analog scale score (VAS) ranging from 0 (not at all bothersome) to 10 cm (extremely bothersome) was used to assess the severity for nasal obstruction. Children under 12 years old were additionally guided by a faces rating scale (FRS) located above the VAS line. FRS is a picture projection technique in which six faces similar to “emoticon” are shown to a child. The first picture is a very happy smiling face and the last is sad and crying [10].

2.2.2. Nasal endoscopy

Three drops (0.39 mg) of topical nasal 0.05% xylometazoline were applied to each nostril. Five minutes later, nasal examination was carried out with a 2.4 mm flexible nasal endoscope. Septum morphology was described according to Mladina classification [11], which includes seven types of NSD (Fig. 1). NSD type 1 is a mild unilateral vertical ridge in the valve area which does not reach the nasal dorsum; therefore it does not change the physiologic valve angle. In NSD type 2, a more emphasized unilateral vertical ridge in the valve area reaches the nasal dorsum, thus narrowing or blocking the physiologic valve angle. NSD type 3 has a unilateral vertical ridge in the deeper areas, near the anterior portion of the middle turbinate. NSD type 4 is an “S”-shaped bilateral vertical

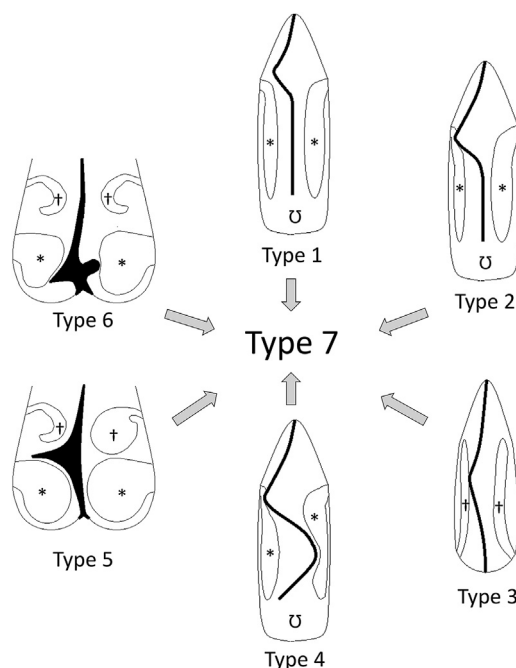


Fig. 1. A schematic depiction of the 7 types of septal deformities according to Mladina's classification. The first 4 types are presented in an axial plane (bird's-eye view), whereas types 5 and 6 are presented in a coronal plane (anteroposterior view) where, *, inferior turbinate; †, middle turbinate; U, choana.

deformity, consisting of type 2 on one side and type 3 on the other. *NSD type 5* is a unilateral septal spur ascending from anterior to posterior, beginning from the part of the intermaxillary wings, sticking laterally and deeply into the nasal cavity. The opposite side of the nasal septum is flat. *NSD type 6* consists of a massive unilateral intermaxillary bone wing with a groove between it and the rest of the septum on this septal side. On the other septal side, there is an anteriorly positioned basal septal crest. *NSD type 7* is a combination of some of the previous six types [11].

In order to simplify analysis, type 1 and 2 NSD were classified as “anterior unilateral NSD”; type 3 and 5 NSD were classified as “posterior unilateral NSD”; and type 4 and 6 were classified as “bilateral NSD”.

Turbinate size was classified in 4 grades (0–3) according to Friedmann's classification [12]: grade 0, normal; grade 1, mild enlargement; grade 2, moderate enlargement with no obvious obstruction; grade 3, severe enlargement with complete occlusion of the nasal cavity.

Adenoid size was scored in 4 grades (1–4) according to Parikh's endoscopic classification [13]: grade 1, adenoids without contact with other anatomic structures; in grades 2, 3, and 4 adenoids are in contact with torus tubarius, vomer, or soft plate (at rest), respectively. Thus, grades 3 and 4 cause bilateral choanal obstruction.

All endoscopies were performed and graded by an ENT specialist (first author; FMS), or by a 4th year ENT resident (second author; MVM) under supervision of the first author.

2.3. Statistical analysis

The data management and statistical analysis was performed using Epiinfo for Windows (Epiinfo™ 7.1.5; Atlanta, USA). Differences among group means were studied by an analysis of variance (ANOVA). The inter-group and intra-group analyses were

performed with two-tailed tests with significance at the $p < 0.05$ level, and data were presented as mean $\pm$ standard deviation. Descriptive analysis was carried out for the demographic characteristics, and a comparative analysis between groups was performed using the χ^2 test. To determine the relationship between different types of septal deformities and medical response or rhinitis severity an unconditional multivariate logistic regression test was performed with the binary outcome of lack of improvement or severe rhinitis as the dependent variable, respectively, and septal deformity types as independent variables.

3. Results

3.1. Demographic data

A total of 150 pediatric patients (mean age 13 ± 2.8 years, females 32.6%) were enrolled in this study. Demographic and clinical data is summarized in Table 1. The two groups were homogeneous in terms of gender, age and allergic sensitization. The majority of patients (70%) were adolescents. According to m-ARIA PER classification, there were no patients with mild rhinitis in our study. The prevalence of severe rhinitis was higher in the NR group compared to the R group. Consequently, the prevalence of moderate disease was higher in the R group. The most frequent comorbidities were asthma and conjunctivitis, without differences between NR and R groups (Table 1).

3.2. Nasal septum deformity

The general prevalence of NSD in our cohort was 87.4%. It was slightly higher in males (89.1%) and adolescents (89.5%) than in females (83.6%) and children (82.2%). Type 4 was the most frequent NSD type (22.6%), followed by type 2 (14.6%), type 6 (13.3%), type 3

Table 1

Demographic and clinical data where: p^* , $p < 0.05$ ANOVA comparison between males and females; p^{**} , $p < 0.05$ Chi square corrected (Yates) comparison between Responders and Non-responders groups; CRS, Chronic Rhinosinusitis.

		Total	Non-responders Group			Responders Group			p^{**}
			Males	Females	p^*	Males	Females	p^*	
Age	N (%)	150 (100)	66 (66)	34 (34)		35 (70)	15 (30)		NS
	Mean (SD)	13 (2.8)	13.27 (2.7)	13.26 (3.1)	0.9	12.65 (2.8)	12.66 (2.9)	0.9	NS
	6–11 years, n (%)	45 (30)	28 (28)			17 (34)			NS
	12–17 years, n (%)	105 (70)	72 (72)			33 (66)			
PER severity (m-ARIA)	Mild, n (%)	0 (0)	0 (0)			0 (0)			0.0006
	Moderate, n (%)	76 (50.7)	37 (37)			39 (78)			
	Severe, n (%)	74 (49.3)	63 (63)			11 (22)			
Comorbidities	Asthma, n (%)	86 (57.3)	54 (54)			32 (64)			NS
	Conjunctivitis, n (%)	63 (42)	47 (47)			16 (32)			NS
	CRS, n (%)	8 (5.3)	8 (8)			0 (0)			NS
Medical treatment received	INS + anti- H_1 , n (%)	64 (42.7)	54 (54)			32 (64)			NS
	INS + LRA, n (%)	86 (57.3)	46 (46)			18 (36)			
Sensitization by skin prick test	Monosensitization, n (%)	99 (66)	63 (63)			36 (72)			NS
	HDM, n (%)	136 (90.6)	86 (86)			50 (100)			NS
	Pollens, n (%)	41 (27.3)	32 (32)			9 (18)			
	Animal dander, n (%)	27 (18)	20 (20)			7 (14)			
	Alternaria, n (%)	9 (6)	6 (6)			3 (6)			
Adenoidal Hyperplasia (Parikh)	Grade 0	67 (44.6)	45 (45)			22 (44)			NS
	Grade 1	59 (39.3)	36 (36)			23 (46)			
	Grade 2	14 (9.3)	9 (9)			5 (10)			
	Grade 3	7 (4.6)	7 (7)			0 (0)			
	Grade 4	3 (2)	3 (3)			0 (0)			
Nasal Septum Morphology	No NSD	19 (12.6)	9 (9)			10 (20)			0.03
	Type 1	16 (10.6)	9 (9)			7 (14)			
	Type 2	22 (14.6)	16 (16)			6 (12)			
	Type 3	18 (12)	9 (9)			9 (18)			
	Type 4	34 (22.6)	29 (29)			5 (10)			
	Type 5	17 (11.3)	9 (9)			8 (16)			
	Type 6	20 (13.3)	16 (16)			4 (8)			
	Type 7	4 (2.6)	3 (3)			1 (2)			

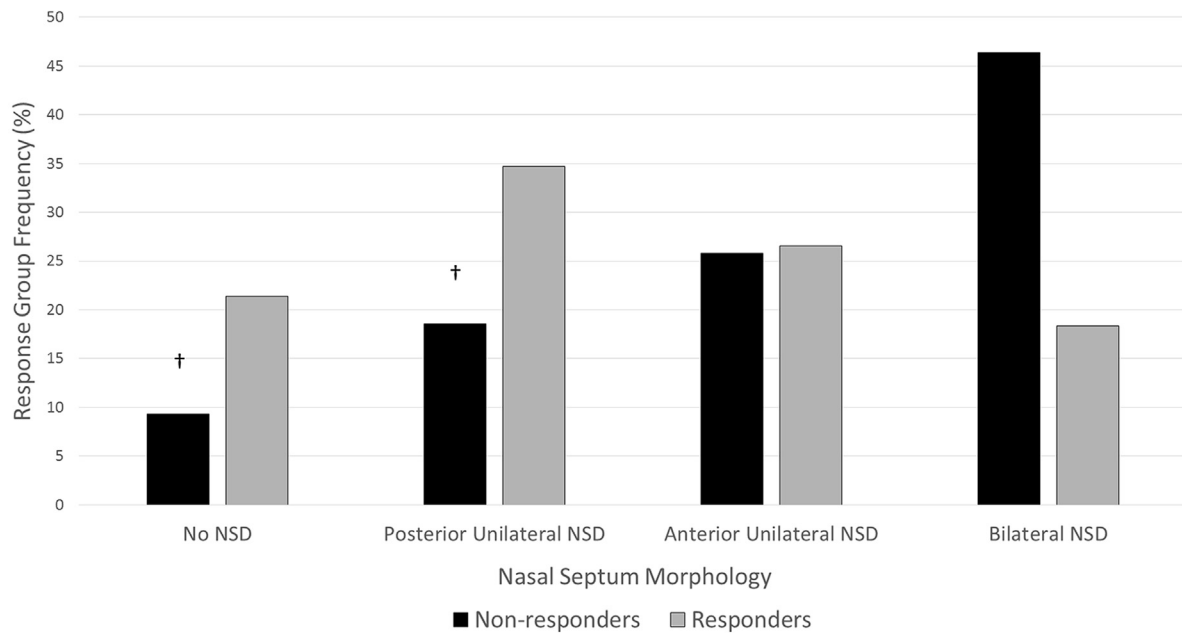
(12%), type 5 (11.3%), type 1 (10.6%), and type 7 (2.6%).

3.2.1. Medical treatment response

Non-responder patients had higher prevalence of NSD types 4, 6, and 2 while responders displayed higher frequency of “no NSD”, type 3, type 5, types 1, and type 7 septal deformities (Table 1). Overall, non-responder patients presented more frequently

bilateral NSD, while responders presented more often “no NSD” or unilateral septum deformities. However, we found no statistically significant differences among treatment response between anterior unilateral and bilateral NSD types (Fig. 2A). When compared with “no NSD”, based on odds ratios, only types 4 (OR = 6.4; $p = 0.005$) and 6 (OR = 4.4; $p = 0.03$) septal deformities were associated with lack of improvement after medical treatment (Fig. 2B).

A



B

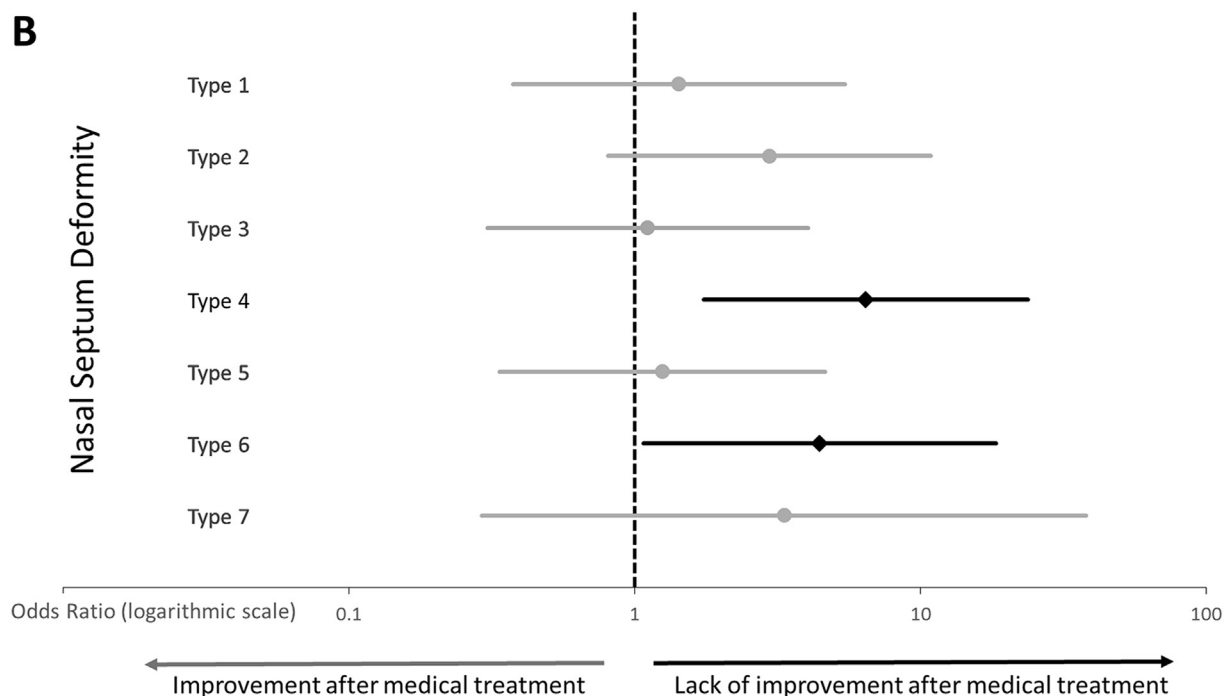


Fig. 2. (A) Prevalence of different nasal septum morphologies in responders (grey columns) or non-responders (black columns) to medical treatment; and (B) logistic regression model associations of different nasal septum deformities (independent variables) with the binary outcome of Medical Response (dependent variable); where, NSD, nasal septal deformity; †, two-tailed Chi square corrected (Yates) $p < 0.05$ difference with Bilateral NSD; ◆ (black lines), $p < 0.05$ association with lack of improvement (risk factor); ● (light grey lines), $p > 0.05$ no association with lack of improvement after medical treatment.

3.2.2. Rhinitis severity

Patients with bilateral NSD presented a higher frequency of severe PER according to m-ARIA classification. Conversely, patients with “no NSD” or with unilateral NSD showed higher prevalence of

moderate PER. However, at NSD intergroup analysis, only comparison of prevalence differences between “no NSD” and bilateral NSD groups reach statistical significance (Fig. 3A). When compared with “no NSD”, only Type 4 NSD (OR = 3.4; $p = 0.03$) was associated

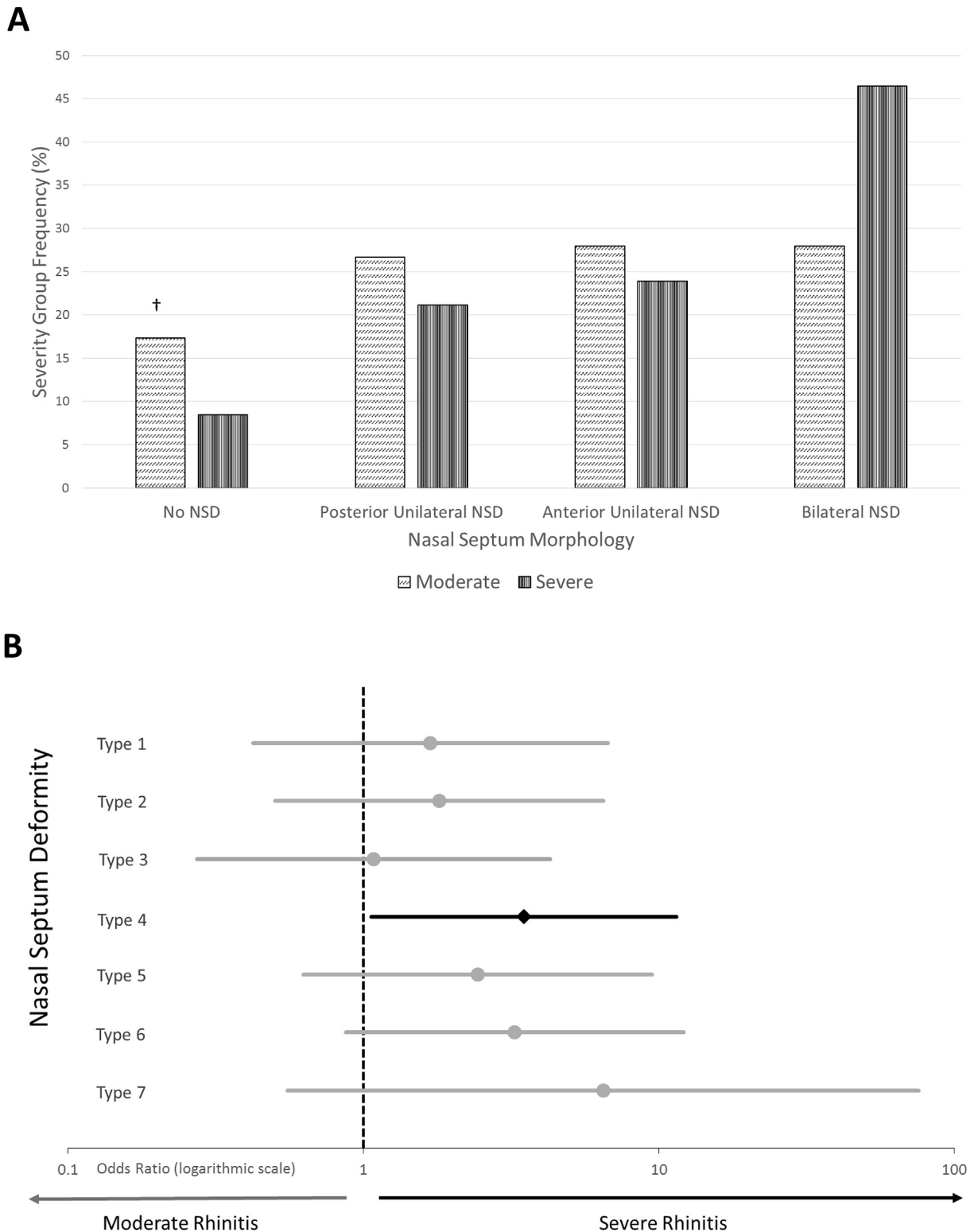


Fig. 3. (A) Prevalence of different nasal septum morphologies in moderate (horizontal lines) and severe (vertical lines) m-ARIA rhinitis severity levels are plotted; and (B) logistic regression model associations of different nasal septum deformities (independent variables) with the binary outcome of Medical Response (dependent variable); where, NSD, nasal septal deformity; †, two-tailed Chi square corrected (Yates) $p < 0.05$ difference with Bilateral NSD; ◆ (black lines), $p < 0.05$ association with severe rhinitis (risk factor); ● (light grey lines), $p > 0.05$ no association with rhinitis severity after medical treatment.

with the presence of severe PER, based on odds ratios (Fig. 3B).

3.2.3. Age and gender

Non-responder adolescents displayed higher frequencies of bilateral and anterior unilateral NSD. However, prevalence comparisons reach significance only between “no NSD” and posterior unilateral NSD with bilateral NSD (Fig. 4A). Responder children displayed higher frequencies of unilateral NSD while responder adolescents presented higher prevalence of “no NSD” and bilateral NSD, with no significant differences among NSD intergroup comparisons (Fig. 4B).

Non-responder males presented higher frequencies of “no NSD”, posterior unilateral and bilateral NSD. Conversely, non-responder females displayed higher prevalence of anterior unilateral NSD (Fig. 4C). Responder females presented higher frequencies of “no NSD” and bilateral NSD while responder males displayed higher prevalence of unilateral NSD (Fig. 4D). We found no significant NSD intergroup gender differences among non-responder or responder patients (Fig. 4C and D).

3.3. Nasal obstruction symptom

Non-responder patients displayed higher nasal obstruction VAS when compared with responders, independently of nasal septum morphology. However, anterior unilateral NSD patients reported higher nasal obstruction VAS than posterior unilateral NSD. Subjects with bilateral NSD displayed higher nasal obstruction VAS than posterior unilateral and “no NSD” patients (Fig. 5A). Patients with obstructive TE and NSD reported higher nasal obstruction VAS than those with no severe TE, independently of their NSD type (Fig. 5B). Overall, adolescents and female patients displayed higher nasal obstruction VAS than children and male patients, respectively, being mean VAS higher for subjects with anterior than posterior NSD, and higher for patients with bilateral NSD than any other type of septal morphology (Fig. 5C and D).

3.4. Adenoidal hyperplasia

All obstructive AH cases belonged to the NR group. However, we found no statistical differences in terms of adenoidal size between responder and non-responder patients (Table 1), nor difference between the presence of obstructive adenoidal hyperplasia and severe turbinate enlargement (43.5% vs 56.43%; $p = 0.9$) or different septum morphologies [no NSD (22.2%), posterior unilateral (11.1%), anterior unilateral (33.3%) and bilateral NSD (33.3%); $p = 0.6$].

3.5. Combined septal deformity and turbinate enlargement

Based on a logistic regression model, the presence of a combined bilateral NSD and severe TE increased more than twentyfold the risk of lack of improvement after medical treatment. Pure severe TE without septal deformity increased the risk of lack of improvement more than tenfold. The presence of bilateral NSD alone, or the combination of anterior unilateral NSD and severe TE, were also associated with lack of improvement. Contrariwise, the absence of severe TE combined with “no NSD” or a posterior NSD was associated with improvement after medical treatment (Table 2).

4. Discussion

The main findings of the present study were: i) there is a high prevalence of bilateral (Mladina's types 4 and 6) and anterior (types 1 and 2) nasal septal deformities in pediatric PER patients not responding to medical treatment; ii) types 4 or 6 NSD increase the

risk of lack of improvement with medical treatment; iii) coexistence of anterior unilateral or bilateral NSD with severe turbinate enlargement increases more than twentyfold the risk of lack of improvement; iv) patients with bilateral NSD present greater rhinitis severity, being type 4 NSD associated with severe PER; v) non-responder adolescents display higher prevalence of bilateral NSD than children; and vi) nasal obstruction VAS is higher for patients with anterior than posterior NSD, and greater for patients with bilateral NSD than any other type of septal morphology.

The prevalence of NSD found in our cohort was considerably higher than the 30% reported in pediatric general population [14] and very close to the 90% reported in adulthood [3]. However, we must emphasize that our sample was mainly constituted by adolescents (70%) with persistent nasal obstruction which are not comparable to healthy general population.

The frequency of different types of NSD in responder patients of our study was similar to that reported in the general population [3]. However, in the NR group the prevalence of bilateral NSD was significantly higher than in responder patients. Conversely, having “no NSD” or a posterior NSD was more frequent in the R group. Moreover, bilateral deformities (types 4 and 6) were associated with lack of improvement after medical treatment. Furthermore, the concomitant presence of a bilateral NSD and severe TE had the worst effect on medical treatment response, while the absence of NSD and TE was associated with improvement.

The anterior portion of the septum forms together with caudal margin of the upper lateral cartilage, the floor of the pyriform aperture and the head of the inferior turbinate, the nasal valve area, which is the narrowest portion of the nasal passage. Therefore, deformities of the valve area, such as an anterior or a bilateral NSD, in an inflamed allergic nose with hyperplastic and swollen turbinate mucosa, may severely impair the dynamics of nasal air flow [15]. Furthermore we might think that these anatomical problems would prevent intranasal steroids entering and distributing correctly in nasal cavities mucosa [16], partially explaining why this patients do not respond to medical therapy. In contrast, a straight septum or a posterior NSD would allow intranasal steroids distribution along inferior turbinate mucosa, with the consequent diminishment of inflammation and turbinate size which would account for clinical improvement after medical treatment.

We previously reported the feasibility of m-ARIA classification to discriminate among moderate and severe treated pediatric patients, and the association of NOD with higher severity of PER [4]. These findings were corroborated in our study, particularly in patients with bilateral NSD. For the same reasons exposed above, bilateral NSD would prevent efficacy of intranasal steroids, therefore associating higher PER severity after medical treatment.

Different worldwide studies point toward an age-related increase on the prevalence of bony NSD deformities, predominating anterior segment deformities resulting from exposure to the effects of trauma which is the most common cause [14]. In our study, we found slightly higher prevalence of NSD in adolescents than children. Moreover, we found a higher frequency of anterior and bilateral NSD in non-responder adolescents when compared to children, probably linked to a progressively increase in risk of exposure to trauma along childhood [17] thus causing an unfavorable response to medical treatment.

In accordance with previous literature [18], we found a slight predominance of male gender in NSD prevalence, probably linked to a more frequent exposure to sport injuries and assaults in males than females [19]. However, we found no significant gender differences among different types of NSD.

Although a relationship between nasal obstruction assessed by endoscopy and perception of nasal obstruction has been reported in children with AR [10], the impact of the nasal cavity area on nasal

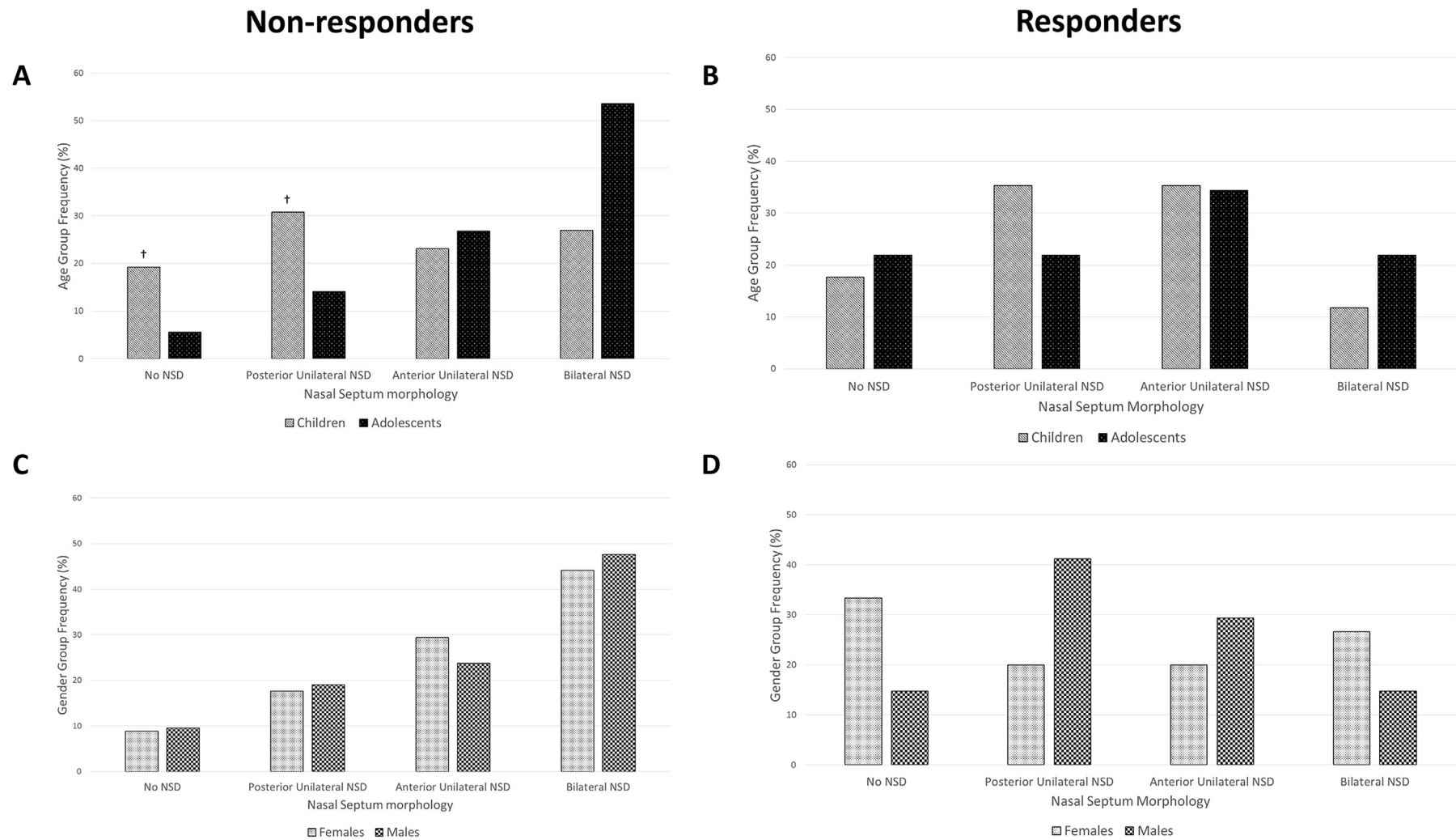


Fig. 4. Prevalence of different nasal septum morphologies in non-responders (**A** and **C**) and responders (**B** and **D**) according to age (children, diagonal striped columns; adolescents, black white dotted columns) and gender (females, white black dotted columns; males, chessboard columns); where, NSD, nasal septal deformity; †, two-tailed Chi square corrected (Yates), $p < 0,05$ difference with Bilateral NSD.

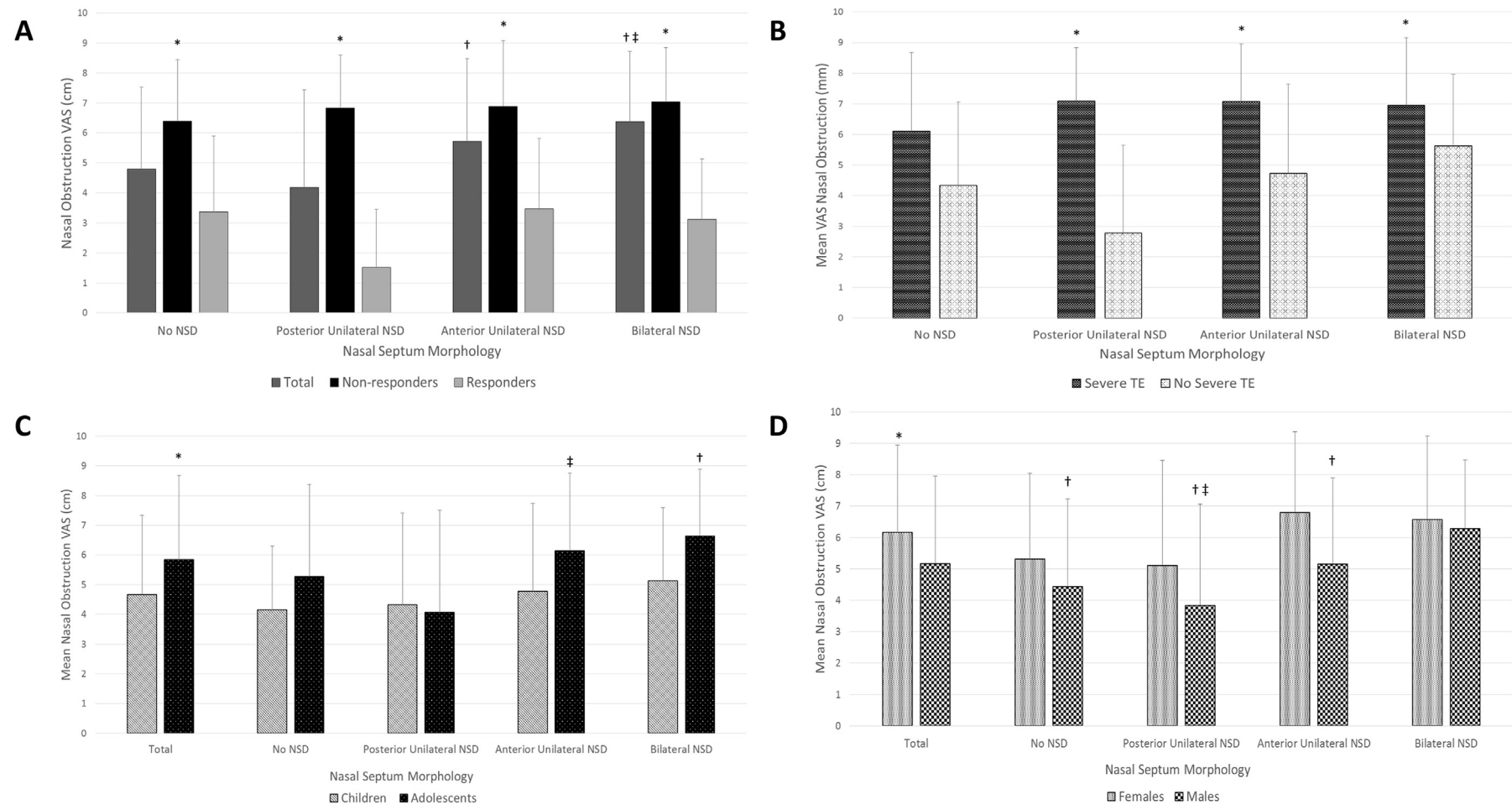


Fig. 5. Nasal obstruction mean VAS scores according to different nasal septum morphologies among: **(A)** responders (grey columns) or non-responders (black columns) to medical treatment, where, NSD, nasal septal deformity; *, $p < 0.05$ ANOVA comparison between non-responders and responders; †, $p < 0.05$ ANOVA comparison with Posterior Unilateral NSD; ‡, $p < 0.05$ ANOVA comparison with No NSD; **(B)** severe (lattice columns) or no severe (dotted rhombus columns) turbinate enlargement. TE, turbinate enlargement; where, *, $p < 0.05$ ANOVA comparison between severe and no severe TE; **(C)** children (diagonal striped columns) or adolescents (black white dotted columns); where, *, $p < 0.05$ ANOVA comparison between children and adolescents; †, $p < 0.05$ comparison with No NSD, Posterior Unilateral NSD and Anterior Unilateral NSD; ‡, $p < 0.05$ comparison with Posterior Unilateral NSD; and **(D)** females (white black dotted columns) or males (chessboard columns); where, *, $p < 0.05$ ANOVA comparison between females and males; †, $p < 0.05$ comparison with Bilateral NSD; ‡, $p < 0.05$ comparison with Anterior Unilateral NSD.

Table 2

Logistic regression model associations of different combinations of septal deformities and turbinate enlargement (independent variables) with the binary outcome of medical treatment response (dependent variable); where, OR, odds ratio; NSD, Nasal septum deformity; TE, turbinate enlargement; dark grey rows, association with lack of improvement after medical treatment (risk factor); white rows, no association with lack of improvement; light grey rows, inverse association with lack of improvement (protective factor).

Endoscopic findings	Lack of improvement after medical treatment			
	Point Estimate	95% Confidence Interval		p
	OR	Lower limit	Upper limit	
No NSD - No Severe TE	0.3011	0.1070	0.8471	0.0229
No NSD + Severe TE	11.2941	2.5827	49.389	0.0013
Posterior Unilateral NSD - No Severe TE	0.3976	0.1815	0.8708	0.0211
Posterior Unilateral NSD + Severe TE	0.3400	0.1000	1.1000	0.9682
Anterior Unilateral NSD - No Severe TE	0.8028	0.3645	1.7678	0.5854
Anterior Unilateral NSD + Severe TE	8.6471	1.1083	67.4679	0.0396
Bilateral NSD - No Severe TE	3.2989	1.4478	7.5166	0.0045
Bilateral NSD + Severe TE	21	2.7704	159.1808	0.0032

airflow is difficult to foresee and children between 6 and 9 years of age have been reported to often underestimate nasal obstruction symptom [20]. In our study adolescents displayed greater nasal obstruction than children. Additionally, non-responder patients reported higher nasal obstruction. Moreover, subjects with bilateral NSD or with septal deformities affecting the nasal valve area reported higher nasal obstruction, irrespective of their age and gender, even greater when severe TE coexisted. These results suggest, in accordance with previous works [21,22], that the differential diagnosis of SD or TE by an ENT specialist through nasal endoscopy might predict children and adolescent's perception of nasal obstruction.

Historically, women have been considered more likely to report worst symptoms and to give poorer self-evaluation of health [23,24]. Additionally, female children between 6 and 14 years old estimate their nasal patency more accurately than males [20]. In our study, female patients displayed higher nasal obstruction than males. However, it has not been established how much these differences can be attributed to cultural factors, learned behavior or to hormonal influences [25].

Several studies have pointed out a correlation between adenoidal hyperplasia and chronic nasal obstruction in children [26,27]. Moreover, AH have been associated with higher rhinitis severity and persistent duration [28]. Although in our study all cases with obstructive AH belonged to the NR group, differences were not statistically significant and we found no association between adenoidal hyperplasia and other endoscopic findings. However, 70% of our cohort was >12 years old when AH incidence is the lowest [29].

In conclusion, examination by nasal endoscopy shows that almost 90% of pediatric PER patients have 1 of the 7 types of septal deformities. Bilateral or unilateral anterior NSD and TE are strongly associated with a poor response to medical treatment. Consequently nasal examination is necessary in these patients to understand the pathology and plan a specific surgical treatment in order to improve nasal obstruction, disease severity, and patient's quality of life.

5. Limitations

i) Our main limitation was the absence of objective tests to better define nasal patency, however, the use of VAS and nasal endoscopy allows, with a fair degree of reliability, to assess nasal obstruction in the absence of rhinomanometry [10,30]; ii) there was a lack of immunologic parameters useful to better understand

the pathophysiological meaning of the clinical data; iii) children sample size ($n = 45$) was relatively low and there was a relatively high proportion of males in our cohort (70%); and iv) in order to verify our results, there is an unmet need to carry out future studies with control groups other than PER patients, e.g. in children with several nasal septum deformities without allergic rhinitis or asymptomatic.

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