# Clinical Communications

## Smell loss is associated with severe and uncontrolled disease in children and adolescents with persistent allergic rhinitis

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***Clinical Implications***

- In pediatric patients with persistent allergic rhinitis, the loss of smell is a clinical marker to identify severe and uncontrolled disease.
- Routine assessment of the sense of smell in clinical practice may improve the management of allergic rhinitis in children and adolescents.

*TO THE EDITOR:*

Smell loss is often experienced by patients with allergic rhinitis (AR). However, few studies, most of them performed in adult population, have assessed olfaction in patients with AR.[1]

We have previously reported that nasal obstructive disorders (NODs), such as nasal septal deformity and turbinate enlargement, cause resistance to medical treatment and worsen quality of life in patients with pediatric persistent AR (PER).[2,3]

The aim of this study was to assess the impact of PER and NOD on the sense of smell of treated pediatric patients and its relationship with response to medical treatment, disease severity, and control.

This was a real-life, prospective, observational study performed in children and adolescents diagnosed with PER and classified according to the modified Allergic Rhinitis and its Impact on Asthma (m-ARIA) guidelines criteria[4] (see the Methods section in this article's Online Repository at www.jaci-inpractice.org). All patients received treatment with daily intranasal corticosteroids (fluticasone or mometasone), and desloratadine or montelukast for 2 consecutive months.

Patients were stratified into children (6-11 years) and adolescents (12-17 years). Nasal examination was carried out with a 2.4-mm flexible nasal endoscope to assess NOD as described elsewhere.[2]

Subjective loss of smell and other nasal symptoms (nasal obstruction, rhinorrhea, itching, and sneezing) were assessed using a visual analogue scale (VAS) ranging from 0 (not at all bothersome) to 10 cm (extremely bothersome) for each individual symptom. Children were additionally guided by the FACES Pain Rating Scale located above the VAS line. The FACES Pain Rating Scale is a picture projection technique in which 6 emoticon-like faces are shown to a child. The first picture is a very happy smiling face and the last is sad and crying[5] (see Figure E1 in this article's Online Repository at www.jaci-inpractice.org).

The presence of self-reported olfactory loss was defined as a VAS score of loss of smell of 1 or more out of 10 cm.

A total VAS (mean of nasal obstruction, itching, sneezing, and rhinorrhea) score of 2 or less of 10 cm was used to define *well-controlled AR*. A total VAS score of 5 or more out of 10 cm was used as a cutoff criterion to define *medical treatment refractoriness* and classify patients into responders ($\leq$5 cm) or nonresponders (>5 cm).[6]

One hundred forty-two patients (99 adolescents; mean age, 13 $\pm$ 2.8 years; 32.3% females) were included. Clinical and demographic characteristics of patients were analyzed with descriptive statistics (see Table E1 in this article's Online Repository at www.jaci-inpractice.org).

More than 60% (n = 87) of patients referred smell dysfunction. Prevalence of self-reported olfactory loss (VAS score > 1 cm) increased with rhinitis severity and in patients with medical treatment refractoriness (Figure 1, *A*). Conversely, prevalence of smell loss was lower in patients with well-controlled AR (26% [n = 6]) than in patients with not-controlled PER (68% [n = 81]; $P = .0003$). No differences were observed in the frequency of smell loss between children (53.4% [n = 23]) and adolescents (64.6% [n = 64]), or between females (67.3% [n = 31]) and males (58.3% [n = 56]).

Smell loss VAS score was higher for nonresponder (3.5 $\pm$ 3.1 cm; $P < .001$) than for responder (0.9 $\pm$ 1.6 cm) patients. In addition, patients with severe rhinitis displayed higher smell loss VAS compared with patients with moderate rhinitis (Figure 1, *B*). Conversely, smell loss VAS score was lower for patients with well-controlled AR (3.0 $\pm$ 2.9 cm; $P = .0001$) than for patients with not-controlled AR (0.4 $\pm$ 0.9 cm).

Figure E2 in this article's Online Repository at www.jaci-inpractice.org shows a moderate correlation between the smell loss VAS score and the average values of total symptom score by VAS for all patients ($R^2 = 0.24$; $P < .001$).

Smell loss VAS score was higher for patients with severe turbinate enlargement than for patients with nonobstructive turbinates, or for patients with a combined obstructive septal deformity and turbinate enlargement. However, we found no differences in terms of smell loss VAS score between patients with or without obstructive septal deviation or adenoidal hyperplasia alone (see Table E2 in this article's Online Repository at www.jaci-inpractice.org), between females (3.2 $\pm$ 2.3 cm) and males (2.2 $\pm$ 1.6 cm), or between children (2.1 $\pm$ 1.5 cm) and adolescents (2.7 $\pm$ 2.0 cm).

Based on odds ratios of the logistic regression analysis (described in this article's Online Repository at www.jaci-inpractice.org), smell loss was associated with medical treatment refractoriness, the presence of severe rhinitis, and the presence of severe turbinate enlargement (Figure 2). Contrariwise, well-controlled AR was inversely associated with olfactory loss. However, we found no association between smell loss and the presence of obstructive septal deformity, obstructive adenoids, asthma, or conjunctivitis.

Receiving-operating characteristic analysis (described in this article's Online Repository at www.jaci-inpractice.org) of the presence of hyposmia (VAS score > 1/10 cm) yielded an area under the curve of 0.677 (61.54% sensitivity, 66% specificity), representing poor accuracy to predict lack of improvement after medical treatment. However, an area under the curve of 0.766

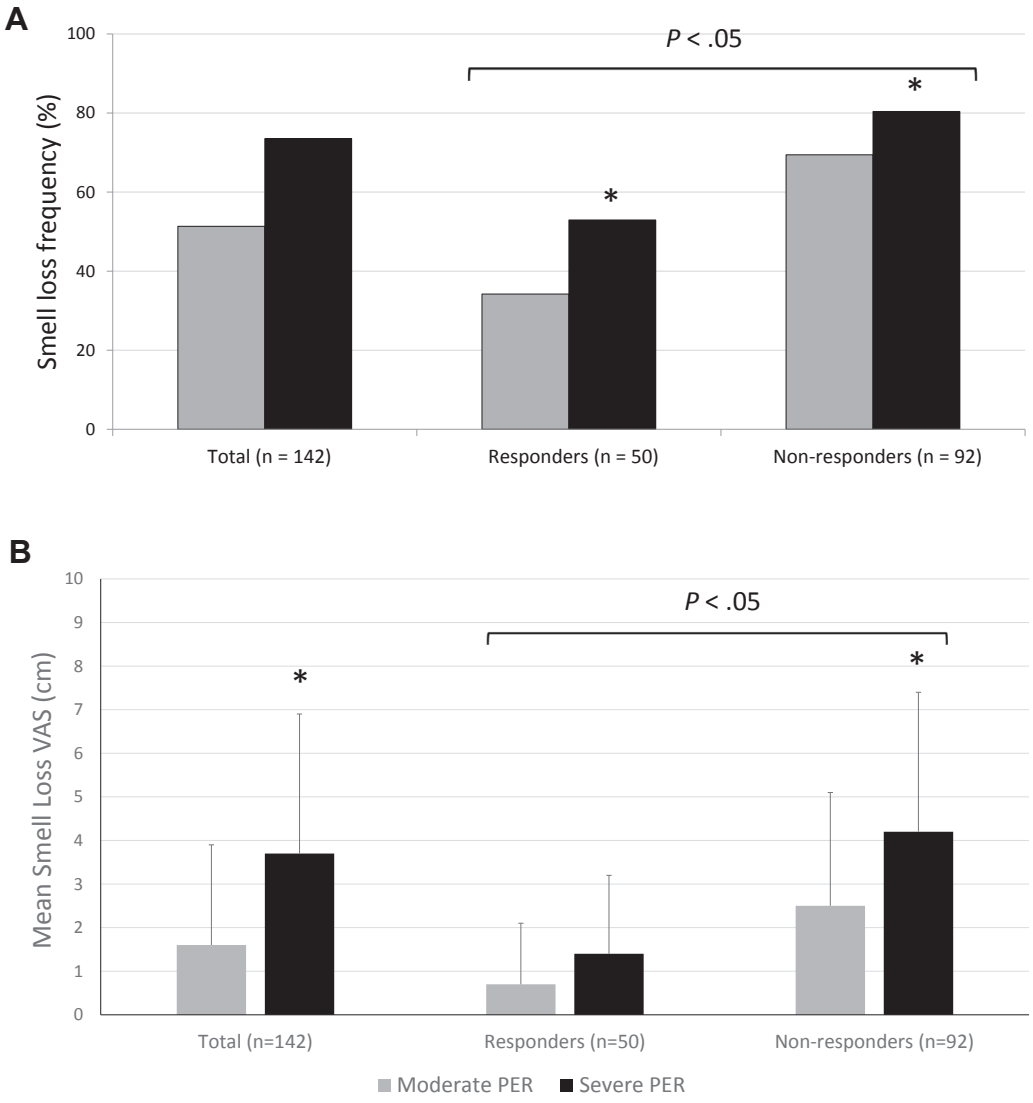


**FIGURE 1. A,** Frequency of smell loss in patients with moderate (gray columns) or severe (black columns) PER (m-ARIA classification) according to treatment response. **B,** Smell loss severity (VAS) in patients with moderate (gray columns) or severe (black columns) PER according to treatment response. *$P < .05$ severe compared with patients with moderate PER (ANOVA).

(68.4% sensitivity, 73.9% specificity) showed a fair accuracy to predict an uncontrolled disease.

To our knowledge, the present study is the first to investigate the relationship between olfactory dysfunction with medical treatment response, and disease severity and control in pediatric patients with AR, using the m-ARIA classification to evaluate rhinitis severity. Significantly, this is the first study to investigate the impact of endoscopic NODs on olfaction in the pediatric population.

AR has been previously associated with moderate olfactory loss in adults[1] and, very recently, in nontreated children.[7] Smell loss seems to be related to a higher duration and severity of rhinitis, probably caused by a mixed etiology in which both nasal obstruction and mucosal inflammation may be responsible.[1]

In the Nasal Obstructive Disorders in Pediatric Allergic Rhinitis (NODPAR) study[2] we have previously demonstrated that NODs are associated with lack of improvement after medical treatment, worse nasal symptoms, and greater disease severity in pediatric patients with PER. The presence of NOD in an inflamed allergic nose with hyperplasic and swollen turbinate mucosa may diminish drug delivery into the nasal cavity. However, in the present study, septal deformity alone was not associated with smell loss, whereas obstructive turbinate enlargement alone or combined with obstructive septal deformity was associated with worse smell loss (VAS). These findings suggest that mucosal inflammation probably thickens the layer odorants need to cross over to bind olfactory receptors at neuroepithelium.

Montoro et al[3] reported that m-ARIA classification could discriminate between moderate and severe AR untreated children. In the present study, we observed that treated pediatric patients with severe PER showed higher frequency and intensity of smell loss when compared with moderate patients, with this