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Dear Editor,

We read the paper of Gilani and Bhattacharyya entitled "Rethinking the relationships between chronic rhinosinusitis and asthma severity [1]". In this retrospective case-control study, authors reported that an increasing severity of asthma classification was associated with chronic rhinosinusitis (CRS) diagnostic in patients with a primary diagnosis of asthma, while the presence of CRS comorbidity in asthma individuals was not associated with an increase of oral corticosteroid use for asthma. Based on their data in 637 patients with both asthma and CRS *versus* 637 controls, they suggested that the unified airway theory may be nuanced [1]. We congratulate the authors for this interesting study investigating a controversial theory linking upper and lower airway disorders. In this letter, we would like to draw attention to an important condition that was not considered in the study, which is the laryngopharyngeal reflux disease (LPRD).

The unified theory suggests a relationship between inflammatory diseases of the upper and lower respiratory tract, specifically CRS and asthma. This theory is mainly based on clinical studies reporting a high prevalence of both conditions in a substantial proportion of asthma or CRS patients [2–4]. From an epidemiological standpoint, the study of association between inflammatory conditions of the lower and upper respiratory tracts needs to carefully consider disorders that may be associated with mucosa inflammation of both anatomical regions. Both allergy and LPRD are disorders that may be frequent in asthma or CRS patients [5–8]. Authors discussed the potential influence of allergic rhinitis on asthma and CRS findings but they did not evaluate the role of LPRD.

The role of LPRD in asthma and CRS has been underestimated for a long-time because the diagnosis of LPRD was mainly based on clinical findings, gastrointestinal symptoms or single- or dual-probe pH-monitoring [6,8–11]. To date, it has been well-established that LPRD is mainly weakly or non-acid, and, consequently, not detected with conventional pH-monitoring. The use of multichannel intraluminal impedance-pH testing without pharyngeal impedance sensors may be insufficient because distal-to-proximal esophageal reflux events may not

reach the pharynx [10–12]. These methodological issues maintain the confusion in the role of LPRD in upper and lower respiratory tract disorders and the potential relationship between CRS and asthma. From a biological standpoint, pepsin was detected in sinus secretions of patients with recalcitrant CRS [6,13] and may lead to chronic inflammation of the respiratory epithelium [14]. Interestingly, similar findings were found in asthma patients with 58.9 % pepsin detection in bronchoalveolar fluids of patients with asthma [15].

The understanding of the relationship between upper and lower inflammatory disorders requires future studies, which must consider the mucosa inflammatory reaction related to allergy and LPRD. For LPRD, the use of hypopharyngeal-esophageal multichannel intraluminal impedance-pH testing remains critical whereas the fluid detection of gastroduodenal enzymes (e.g. pepsin, bile salts) is likely to improve the understanding of the relationship between CRS and asthma. According to its high prevalence, LPRD could be found to be linked to both CRS and asthma.

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