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LETTER TO THE EDITOR Open Access

A EUFOREA comment on a lost comorbidity of asthma

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Abstract

"Epidemiology of comorbidities and their association with asthma control" (Tomisa, G., Horváth, A., Sánta, B. et al. Epidemiology of comorbidities and their association with asthma control. *Allergy Asthma Clin Immunol* 17, 95 (2021). https://doi.org/10.1186/s13223-021-00598-3) is an interesting paper reflecting data collection from more than 12,000 asthmatic patients in Hungary regarding their condition and associated comorbidities. We found it valuable that the paper provides an overview of asthma comorbidities not usually considered in similar reports. Nevertheless, we believe that chronic rhinosinusitis (CRS) with or without nasal polyps (CRSwNP or CRSsNP) should have been listed due to its high incidence and prevalence, its association with asthma which is also endorsed in both GINA and EPOS, as well as in several peer-reviewed scientific papers, and to reflect the role of this comorbidity in poor control and a most severe presentation of asthma for the patient. Consequently, several targeted therapies (especially monoclonal antibodies) used for several years in severe forms of asthma are now indicated also for the effective treatment of nasal polyps.

Keywords Asthma, Comorbidities, Allergic rhinitis, Chronic rhinosinusitis with nasal polyps, Chronic rhinosinusitis without nasal polyps

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Main text

The paper by Tomisa et al. [1] describes the prevalence of several common comorbidities of asthma in relation to patient characteristics (age, gender and body mass index [BMI]) and their association with asthma control in a large, specialist-managed patient population.

Although just cryptically mentioned in this paper and presumably hidden under the name of seasonal rhinitis/perennial rhinitis (according to ARIA intermittent or persistent), CRS is a common and prevalent disease imposing a significant health problem that is known to affect up to 10.9% of the global population, while severe CRSwNP is present in approximately 1–2% of the European population [2]. The prevalence of asthma in CRSsNP patients is 21.2%, and 44.9% for CRSwNP patients [3]. Both lead to a significant burden on society in terms of healthcare consumption and productivity loss [4–6].

CRSwNP is an invalidating disease characterized by type 2 inflammation with a major impact on quality of life of those severely affected and often associated with comorbidities such as asthma, allergies, sleep-disordered breathing and non-steroidal anti-inflammatory drugs exacerbated respiratory disease (N-ERD) [7, 8].

Despite a substantial burden and affect of quality of life in individuals (extensively confirmed with validated questionnaires including the general health EQ-5D [9, 10] and SF36 [11, 12]), their relatives, as well as society and health economics, CRS often remains un-diagnosed, and thus under-estimated, and consequently under- or mistreated [13].

The work by Tomisa et al. does not give a prominent role to rhinitis or CRS to influence the control or severity of asthma. However, given the anatomic, epidemiologic and pathophysiologic connections between the upper and lower airways [14–16], the concept of united airway disease (one airway – one disease, as exposed in EPOS and GINA) has gained more interest in the past years, leading to better diagnosis and therapeutic approaches in patients with such problems [17–19]. Lower airway inflammation often co-exists in CRS, with up to two-thirds of those patients affected by comorbid asthma, COPD or bronchiectasis [20–23].

Several immune mechanisms have been reported to be involved in the naso-bronchial interaction in patients with global airway disease. Type 2 inflammation, present in the majority of adult asthma patients, has also been demonstrated in their sinonasal secretions [24, 25]. In addition, challenging either compartment of the airways has been shown to induce inflammation in the counterpart [26].

More recently, targeted treatment options with biologics provided further insight into the underlying mechanisms and relationship between upper and lower airways in patients with asthma and CRSwNP. Therefore, it is not surprising that biological treatments targeting inflammatory pathways and molecules such as IL-4, IL-13, IL-5 and IgE in both upper and lower airway T2-high inflammation are effective in both asthma and CRSwNP [27–31].

Further evidence for associations between upper and lower airway compartments has shown that co-existent CRS increases the patient´s risk of exacerbations even if they have few asthma symptoms, and it is associated with a more severe asthma course, especially in patients with nasal polyps [32, 33].

Like other comorbidities such as obesity, sleep apnoea, and anxiety, the presence of AR or CRS are among the criteria for difficult-to-treat asthma [34].

In fact, the HELIUS study showed CRS to be associated with adult-onset asthma [35] and the Asthma Clinical Research Network demonstrated that CRS is associated with increased risk of asthma exacerbations [36].

Chen et al. [37] identified patients newly diagnosed with asthma in Taiwan and analyzed the incidence of CRS in that population. After adjustment for gender, age and medical comorbidities, they showed that asthma is an independent predictor of CRS, with or without nasal polyps (OR: 2.58 for CRSsNP).

In addition, endoscopic sinus surgery in asthma has been reported to improve multiple clinical asthma parameters [38]. The frequency of severe asthma exacerbations decreased in 84.8% (95% CI, 76.6–93.0%) of patients and the number of hospitalizations decreased in 64.4% (95% CI, 53.3–75.6%). Decreased use of oral corticosteroids was seen in 72.8% (95% CI, 67.5–78.1%) of patients; inhaled corticosteroid use decreased in 28.5% (95% CI, 22.6–34.5%) and bronchodilator use decreased in 36.3% (95% CI, 28.9–43.7%) of patients [39].

Unable to access the questionnaire applied, we can only speculate why CRS is not explicitly mentioned in this paper. Possibly, the sample consisted of patients with allergic asthma, which is associated with AR more than CRS and not with late-onset non-allergic asthma.

However, we found it very interesting that this work is based on a previous one (Tomisa G et al. Prevalence and impact of risk factors for poor asthma outcomes in a large, specialist-managed patient cohort: a real-life study. *J Asthma Allergy*. 2019; 12:297–307. https://doi.org/10.2147/JAA.S211246), in which the same sample was used, and AR and CRS are named as the first comorbidity found and also remarked as one of the main risk factors for uncontrolled disease.

Abbreviations

AR	Allergic rhinitis
CRS	Chronic Rhinosinusitis
CRSsNP	Chronic Rhinosinusitis without Nasal Polyps
CRSwNP	Chronic Rhinosinusitis with Nasal Polyps
N-ERD	NSAIDs Exacerbated Respiratory Disease
NSAID	Non-steroidal anti-inflammatory drug

COPD	Chronic obstructive pulmonary disease
EPOS	European Position Paper on Rhinosinusitis and Nasal Polyps
GINA	Global Initiative for Asthma

Authors' contributions

DC: Has made substantial contributions to the conception and design of the work, has contributed to the interpretation of data, has drafted the work, and substantively revised it. Has also approved the submitted version and has agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated, resolved, and the resolution documented in the literature.
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ZD: Has made substantial contributions to the conception and design of the work. Has contributed to the interpretation of data and has critically revised the work. Has also approved the submitted version and agreed to be personally accountable for the author's contributions and to ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated, resolved, and the resolution documented in the literature.
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SL: Has made substantial contributions to the conception and design of the work. Has contributed to the interpretation of data and has substantively revised the work. Has also approved the submitted version and agreed to be personally accountable for the author's contributions and to ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated, resolved, and the resolution documented in the literature.
EVS: Has made substantial contributions to the conception and design of the work. Has contributed to the interpretation of data and has substantively revised the work. Has also approved the submitted version and agreed to be personally accountable for the author's contributions and to ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated, resolved, and the resolution documented in the literature.
GS: Had the original idea for this paper and has made substantial contributions to the design of the work. Has contributed to the interpretation of data and has substantively revised the work. Has also approved the submitted version and agreed to be personally accountable for the author's contributions and to ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated, resolved, and the resolution documented in the literature.

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Consent for publication
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Competing interests
Diego Conti is the academic manager at EUFOREA. He has no competing interest to declare. Peter Hellings is consultant and recipient of lecture fees and/or research grants from Sanofi, Regeneron, Novartis, GSK, ALK, and Viatris. Zuzana Diamant received in the past three years speaker fees or honoraria or serving on advisory boards or as a consultant from Antabio, Boehringer Ingelheim, Foresee Pharmaceuticals, GlaxoSmithKline, QPS-Netherlands, Sanofi-Genzyme-Regeneron, all outside the submitted work. Leif Bjermer has no competing interest to declare in relation to this work. Milos Jesenak reports receiving consultancy/speaker honoraria from CSL Behring, SOBI, Novartis, GSK, Sanofi, Viatris, and Takeda Pharmaceutical Co. Ltd.; and serving as a principal investigator for clinical trials sponsored by Takeda, Mundipharma, Octapharma, BioCryst Pharmaceuticals, Inc. and Pharming Group NV. Vibeke Backer has no competing interest to declare in relation to this work. Wytske Fokkens has no competing interest to declare in relation to this work. Susanne Lau has received honoraria for lectures and AD Boards from Sanofi-Aventis, DBV, Allergopharma, ALK, Leti, GSK, and Leo Pharma in the last three years. Elizabeth Van Staeyen is the Scientific Communications & Advocacy Manager at EUFOREA. She has no competing interest to declare. Glenis Scadding is a Board member of EUFOREA. She has received remuneration from Sanofi Regeneron and has undertaken trials for GSK.

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