OVERLAP OF BIOMARKERS AND TYPE-2 COMORBIDITIES IN AN INTERNATIONAL SEVERE ASTHMA POPULATION

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Background

- Severe asthma: a subgroup of patients with asthma having a high disease burden; difficult to treat, requiring extensive diagnostic evaluation and therapeutic intervention for disease control.[1]
- Severe asthma is a complex, heterogeneous condition with multiple phenotypes.
- Biomarkers that are indicative of underlying pathological processes may identify phenotypes of asthma and even the underlying endotypes, determine prognosis, and predict or monitor treatment responses.
- Biomarkers of asthma have been reported to overlap considerably.[2]

Rationale

- The pattern of overlap and discordance of biomarkers have not been previously reported in an international cohort of patients with varying features of severe asthma.
- Assessing biomarkers on a global scale was previously hindered by the lack of uniformity in severe asthma definition and data collection among national and regional registries.

Aim

- To describe the distribution of common biomarkers, including blood eosinophil count (BEC), immunoglobulin E (IgE) and fractional exhaled nitric oxide (FeNO), and the pattern of Type-2 (T2) comorbidities (allergic rhinitis, chronic rhinosinusitis and nasal polyps) in an international severe asthma population.

Methods

Design

- Cross-sectional review of severe asthma patients on GINA Step 5 or uncontrolled on GINA Step 4, enrolled in the International Severe Asthma Registry (ISAR) between September 2018 to January 2019.

The International Severe Asthma Registry (ISAR)

- The first global effort to harmonise prospective data of adult severe asthma patients across the globe (http://isaregistries.org).
- An on-going initiative with ever-growing number of participating registries; currently over 200 centres from 10 registries are participating.

Sample Size

- 776 adult patients with severe asthma were included from 8 countries

Figure 1. Number of patients enrolled from national and regional severe asthma registries

Baseline clinical characteristics reviewed

Characteristics	Biomarkers	T2 Comorbidities
Age	Blood Eosinophil Count (BEC) • Low: <300 cells/µl • High: ≥300 cells/µl	Allergic Rhinitis
Gender	Immunoglobulin E (IgE) • Low: <100 IU/ml • High: ≥100 IU/ml	Chronic Rhinosinusitis
Age of asthma onset • Late onset: ≥18 years	Fractional Exhaled Nitrogen Oxide (FeNO) • <25 ppb • ≥25 ppb	Nasal Polyps

Results

Overlap of biomarker levels

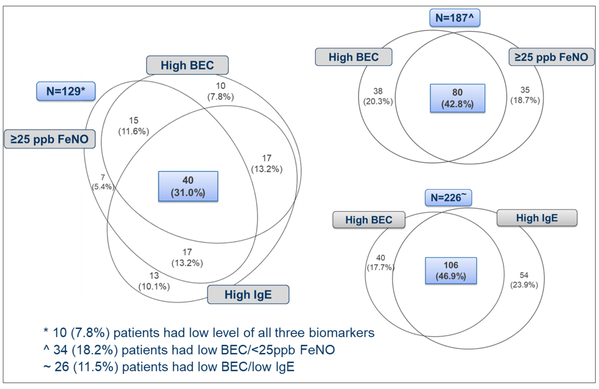

Figure 2: Overlap of biomarkers in a global severe asthma population

- A total of 689 severe asthma patients had at least BEC or FeNO or IgE records available; 129 (18.7%) patients had a valid value for all three biomarkers.
- 31.0% of the patients (n=40) were in the high BEC/ ≥25ppb/ high IgE cluster.
- Majority of the patients (n=89; 69%) had high levels for at least 2 biomarkers.

Characteristics of severe asthma phenotypes by biomarkers

Blood Eosinophil Count		Low		High		Overall
Fractional Exhaled Nitrogen Oxide (ppb)		<25	≥25	<25	≥25	
N		34	35	38	80	187
Age, Mean (SD)		54.3 (11.5)	52.0 (12.6)	55.9 (15.1)	51.4 (12.0)	53.0 (12.7)
Female	Non-missing, N	28	26	38	70	162
	N (%)	18 (64.3)	13 (50.0)	25 (65.8)	39 (55.7)	95 (58.6)
Late-onset (≥18 years)	Non-missing, N	32	32	35	76	175
	N (%)	27 (84.4)	24 (75.0)	29 (82.9)	65 (85.5)	145 (82.9)
Comorbidities						
Allergic Rhinitis	Non-missing, N	27	28	20	54	129
	N (%)	19 (70.4)	20 (71.4)	16 (80.0)	**50 (92.6)**	105 (81.4)
Chronic rhinosinusitis	Non-missing, N	30	28	32	67	157
	N (%)	20 (66.7)	**20 (71.4)**	8 (25.0)	35 (52.2)	83 (52.9)
Nasal polyps	Non-missing, N	33	30	38	76	177
	N (%)	12 (36.4)	12 (40.0)	18 (47.4)	**46 (60.5)**	88 (49.7)

Blood Eosinophil Count		Low		High		Overall
Immunoglobulin E		Low	High	Low	High	
N		26	54	40	106	226
Age, Mean (SD)		54.4 (12.5)	50.2 (12.6)	53.7 (11.9)	53.0 (13.9)	52.6 (13.1)
Female	Non-missing, N	19	47	38	104	208
	N (%)	12 (63.2)	28 (59.6)	21 (55.3)	60 (57.8)	121 (58.2)
Late-onset (≥18 years)	Non-missing, N	25	48	39	99	211
	N (%)	21 (84.0)	31 (64.6)	31 (79.5)	82 (82.8)	165 (78.2)
Comorbidities						
Allergic Rhinitis	Non-missing, N	21	39	18	72	150
	N (%)	15 (71.4)	30 (76.9)	16 (88.9)	**66 (91.7)**	127 (84.7)
Chronic rhinosinusitis	Non-missing, N	23	47	37	93	200
	N (%)	**15 (65.2)**	22 (47.8)	17 (45.9)	50 (53.8)	104 (52.0)
Nasal polyps	Non-missing, N	25	47	40	101	213
	N (%)	9 (36.0)	15 (31.9)	20 (50.0)	**52 (51.5)**	96 (45.1)

- Mean age was the highest in high BEC/<25ppb FeNO cluster and lowest in the low BEC/high IgE cluster.
- Allergic rhinitis and nasal polyps were most prevalent in the high BEC/≥25 ppb FeNO and the high BEC/high IgE clusters.
- Chronic rhinosinusitis was most prevalent in the low BEC/ ≥25 ppb FeNO (71.4%) and the low BEC/low IgE cluster (65.2%).

Conclusions

- We highlighted combinations of key patient characteristics and biomarker clusters in an international sample of severe asthma patients from the ISAR database.
- These clusters can serve as a basis for identification of specific phenotypes of severe asthma.

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Conflict of interest statement:

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