The Demographic and Clinical Characteristics of Eosinophilic and non-Eosinophilic Phenotypes of Severe Asthma in International Severe Asthma Registry (ISAR)

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Introduction: Severe asthma is a heterogenous disease with imprecise sub-classification into phenotypes based on clinical, functional or inflammatory parameters. Currently, there is a lack of information on overlapping and distinct characteristics of eosinophilic (EOS) and non-eosinophilic phenotypes in a global, real-life severe asthma cohort. This study aimed to describe and compare the baseline demographic and clinical characteristics between EOS and non-EOS phenotypes of severe asthma.

Methods: Adult severe asthma patients on Global Initiative for Asthma (GINA) Step 5 treatment or with uncontrolled disease on GINA Step 4 treatment enrolled into the International Severe Asthma Registry (ISAR) were included in this study. Data were collected using standardized electronic case report forms from 11 countries between January 2015 – September 2019. Patients with available blood eosinophil count (BEC) were included and were categorised into EOS (most-likely and likely groups only) or non-EOS phenotype (unlikely only) per a pre-defined gradient eosinophilic algorithm. This algorithm was developed by systematic literature review and consensus of severe asthma experts comprising the ISAR steering committee. The current abstract shows the sensitivity results from a modified algorithm after excluding age of onset (Table 1). For patients on Anti-IL5/5R, pre-biologic BEC was used. Demographic and clinical characteristics were defined at baseline (i.e. one year prior or closest to date of BEC measurement). Chi-square, Mann-Whitney U, or two-sample tests of proportions were applied to determine any significant differences (p-value<0.05) between groups.

Results: Of the 1,716 patients included in this study, 90% were categorised as EOS phenotype. As shown in Table 2, compared to the EOS group, proportion of females were significantly higher in the non-EOS group. A significantly higher proportion of patients with fixed airways obstruction (post-bronchodilator $FEV_1/FVC<0.7$) was found in the EOS group. Anti-IgE and ICS/LABA/LTRA prescriptions in the baseline period were reportedly higher for the patients in non-EOS group. No significant differences were observed across the 2 groups in terms of age of asthma onset, comorbidities, IgE levels, asthma control and exacerbations.

Conclusion: These results provide an overview of the similarities and differences in demographic and clinical characteristics of asthma phenotypes. These findings are valuable for all stakeholders (i.e. providers, healthcare payors and scientific community) in order to move us one step closer to the goal of precision medicine in severe asthma. These results should be further applied to another severe asthma population to assess their generalizability.

Table 1. Gradient eosinophilic algorithm

HIGHEST BEC[£] (CELLS/µl)*	**TREATMENT OR CLINICAL CHARACTERISTIC**	**EOS PHENOTYPE**	**PATIENTS (N)**
≥300		Most-likely	1196
	Anti-IL5/5R[±]	Most-likely	178
≥150 - <300	mOCS[©]	Most-likely	37

HIGHEST BEC[£] (CELLS/µl)*	TREATMENT OR CLINICAL CHARACTERISTIC	EOS PHENOTYPE	PATIENTS (N)
	Presence of nasal polyp (NP) and elevated FeNO[¥]	Most-likely	7
	NP or elevated FeNO	Likely	45
	Neither NP nor elevated FeNO	Least-likely	69
<150	mOCS	Likely	75
	NP or elevated FeNO	Least-likely	40
	Neither NP nor elevated FeNO	Unlikely/ Non-EOS	69
[£] blood eosinophil count; *independent criteria specified in each row; [±]Anti-interleukin-5/5-Receptor; [©] Maintenance OCS; [¥] Fractional exhaled nitric oxide ≥25ppb			

Table 2. Demographic and clinical characteristics of EOS vs Non-EOS phenotypes

CHARACTERISTIC	Non-EOS (N=69)	EOS (N=1538)	p-value
Gender	68	1530	
Female, N(%)	22 (81.5)	961 (62.8)	0.001[±*]
Age	63	1478	
Mean (SD)	49.1 (14.7)	52.3 (13.8)	0.145[@]
Age of Onset	64	1394	
Mean (SD)	27.4 (18.4)	28.9 (18.1)	0.637[@]
<18	23 (35.9)	424 (30.4)	
18-29	9 (14.1)	271 (19.4)	0.465[±]
≥30	32 (50.0)	699 (50.1)	
Comorbidities, N (%)[$]			
Chronic rhinosinusitis without NP[π]	37	798	
Yes	18 (48.6)	188 (38.8)	0.240[±]
Eczema	56	1243	
Yes	7 (12.5)	105 (8.4)	0.291[±]
Allergic rhinitis	42	837	
Yes	27 (64.3)	547 (65.3)	0.887[±]
Asthma control, N(%)	62	1269	
Poorly controlled asthma	38 (61.3)	760 (59.9)	0.647[±]
Not well controlled	11 (17.7)	186 (14.7)	
Well controlled	13 (21.0)	323 (25.4)	
Exacerbations, N(%)	59	1316	
Mean (SD)	3.0 (3.8)	3.5 (3.8)	0.297[@]
0	16 (27.1)	337 (25.6)	0.140[±]
1	12 (20.3)	160 (12.2)	
≥2	31(52.5)	819(62.2)	
IgE[β], N(%)	41	1247	
<150	16 (39.0)	477 (38.2)	0.590[±]
150-400	14 (34.1)	351 (28.1)	
>400	11 (26.8)	419 (33.6)	
Post-BD FEV1/FVC[Ω] Ratio	31	578	
<0.7, N(%)	9 (24.3)	271 (46.9)	0.007[~*]

CHARACTERISTIC	Non-EOS (N=69)	EOS (N=1538)	p-value
Medication, N(%)			
Anti-IgE	21 (30.4)	204 (13.3)	0.000$^{\pm}$
Macrolide	6 (8.7)	77 (5.0)	0.176$^{\pm}$
ICS+LABA+LAMA$^{\alpha}$	23 (33.3)	494 (32.1)	0.833$^{\pm}$
ICS+LABA+LTRA$^{\infty}$	31 (44.9)	433 (28.1)	0.003$^{\pm *}$

$^{\$}$based on medical history; $^{\pi}$Nasal polyps; $^{\beta}$Immunoglobulin E; $^{\Omega}$Post-Bronchodilator ratio of Forced Exhaled Volume in the first second and Forced Vital Capacity**;** $^{\pm}$Chi-square, $^{@}$Mann-Whitney, $^{\sim}$two-sample test of proportions, *p-value<0.05; $^{\alpha}$Inhaled corticosteroid, long-acting beta agonist, long-acting muscarinic antagonists; $^{\infty}$leukotriene receptor antagonists