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Editorial

Clinical Asthma Phenotypes; A Challenging but Promising Spectrum

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Editorial

Asthma is a common, chronic and heterogeneous syndrome, affecting people of all ages, all races and both sexes. In recent years, it has become clearly apparent that asthma management must be individualized and tailored not only to the severity of the disease but also, importantly, to the phenotypic characteristics of the patient [1].

Researchers have tried to define asthma phenotypes based on its clinical, physiologic and cellular parameters. Interestingly, tailoring asthma therapy according to the clinical phenotype is particularly crucial since asthma diagnosis is based mainly on clinical basis. Classification methods based on clinical features included those defined by symptoms (age at onset, natural history, severity), triggers (allergic versus non-allergic, exercise, viral), and treatment response [2].

Other clinical asthma phenotypes included cough variant asthma and obese asthma phenotype [3].

The addition of a genetic or blood biomarker could move a phenotype towards the evolving term of "endotype", defined as a sub grouping of disease associated with distinct functional or pathologic mechanisms [4]. Thus, verification of clinical asthma phenotypes by correlating them with their underlying genotypes and certain airway inflammatory biomarkers is extremely pivotal.

We have previously hypothesized an approach to classify asthma phenotypes based on validated symptomatology [Shortness of Breath (SOB), cough, wheezy phenotypes] in correlation with cytokine profile and airway inflammatory biomarkers aiming to detect their impact on asthma treatment [5]. Our study described a wide variability in the baseline characteristics of the proposed clinical phenotypes in which the **SOB phenotype** group were found to have significant increase of total sIgE, soluble interleukin-2 receptor serum concentration and decrease in FEV1 in comparison to both cough and wheezy groups. Other characteristics included older age (>10 years), male gender, and longer disease duration with negative family history of asthma. Whereas, **cough phenotype** group was found to have an eosinophilic pattern, younger age (<10 years), female gender, and shorter disease duration, with positive family history of Asthma. On the other aspect, a mixed IgE and eosinophilic pattern were noticed in the **wheezy phenotype** group. This wide variation in the features of each clinical asthma phenotype had its implication on treatment response where the SOB group responded to fluticasone alone, the cough group responded to montelukast alone, and the wheezy group responded to both medications.

Numerous studies suggested that genetic factors may mediate a large part of heterogeneity in response to asthma medications among asthmatics. Further, Cytokine gene polymorphisms were found to affect the serum levels of cytokines by influencing transcriptional regulation [6,7]. Thus in another recent study, we explored the genetic profile of the proposed clinical asthma phenotypes, in addition to their cytokine profile and other airway biomarkers [4]. The proposed clinical phenotypes included cough phenotype, SOB phenotype, and cough with SOB phenotype. Single nucleotide polymorphism of IL4RA 175V and IL4C-590T were studied in the different clinical phenotypes. We found that **asthma as a group** had AGheterozygosity genotype of IL4RA 175V, whereas, **cough with SOB** group showed AA and GGhomozygosity genotype. Further, cough with SOB group showed significant elevated serum levels of IL-9 among those with IL-4RA AA and GG genotypes in comparison to the other phenotypes with similar genotypes. In addition, this group showed significant increase in serum IL-9 and peripheral eosinophilic percentage compared to cough group.

Also, the study recognized a specific **cough phenotype** among Egyptian asthmatics characterized by a significant decrease in FEV1/FVC ratio and a significant increase in serum levels of IL-17 among patients with CC homozygote variant of IL-4C 590T compared to patients with CT heterozygote variant. Finally, the **SOB phenotype** group showed significant increase in FENO values in comparison to the other groups. In addition, it revealed significant increase in serum levels of IL-17 among patients with CC homozygote variant of IL-4C 590T compared to patients with CT heterozygote variant.

Asthmatic's perception of asthma symptoms and degree of severity has long been recognized to be important in the effective management of asthma [8,9]. Children's dependence on parents complicates the linkage between symptom perception and appropriate intervention. Also, failure to treat may reflect the perception by the child or interpretation and action by the adult caregiver [8]. Thus, accurate verification of clinical asthma phenotypes and appropriate follow up of patient's symptoms to ensure their persistence and constancy are challenging and crucial. In addition, correlating the observable clinical profiles with the underlying genetic and biological factors is pivotal.

Clinical asthma phenotyping is a broad interesting spectrum which could have significant implications on tailoring asthma management if applied accurately. Further studies are required to verify those clinical asthma phenotypes and define their genetic and pathological characteristics.

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