

Do gender and puberty influence allergic diseases?

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To the Editor:

The differences between biological sex, gender identity and its impact on health can have significant implications for the prevention, screening, diagnosis and treatment of various diseases, including allergic diseases. Gender and sex are multidimensional, interactive, intertwined and are sometimes difficult to separate, so the use of the two words (gender and sex) can help to understand the social, cultural and biological context.¹

During childhood (0-10 years) prevalence of allergic rhinitis (AR) is higher among boys than girls. On the contrary, during adolescence (11-17 years) females display higher prevalence of AR compared to their male counterparts. However, when they reach adulthood (18-79 years), there is no difference in prevalence between genders. The same pattern occurs, even more pronounced, for prevalence of coexisting AR and asthma.^{2,3}

In the first year of life, rates of allergic sensitization (specific IgE production) are significantly higher in males, as are serum levels of total IgE. In this age group, serum levels of total IgE appear to suffer a strong genetic influence and may not predict levels of total IgE in the same individual later in life. Increased levels of IgE and higher prevalence of sensitization in boys remains until adolescence. After puberty, total serum and allergen-specific IgE levels in men are thought to remain higher or comparable to those in women. In adulthood, IgE levels decrease in both genders. In addition to changes during life, IgE levels are also influenced by menstrual periods and pregnancy, suggesting the participation of sex hormones in their regulation.⁴

A recent analysis performed in 4,500 brazilian children aged 13-14 years has shown that females not only have a higher prevalence of AR compared to males, but also of allergic rhinoconjunctivitis (ARC), asthma, allergic conjunctivitis (AC) and atopic dermatitis (AD) (Figure 1, A). Interestingly, there is an opposite allergic sensitization pattern with respect to gender, with more allergic sensitization in boys than in girls (Figure 1, B). Moreover, it has also been observed that monosensitization is more frequent in females, while polysensitization is more common in males.⁵

A global meta-analysis showed sex-related differences in rhinitis prevalence with a switch at around puberty from a male predominance to a female predominance. For the prevalence of rhinitis in adulthood, this evaluation found no predominance in either males or females, although the number of studies was low. In the future, it will be mandatory to perform longitudinal studies in which the follow-up is continued into adulthood.⁶

A meta-analysis of longitudinal birth cohorts showed a sex shift from higher incidence in boys before puberty towards a rather sex-balanced incidence after puberty onset. The elevated risk of asthma and rhinitis incidences in teenage girls should lead to more consideration of a sex-specific and age-specific focus on

diagnosis and treatment of respiratory diseases.⁷

The complexity of most allergic diseases is based on a dynamic heterogeneous combination of hyperresponsiveness, dysregulated immune response, chronic inflammation, and tissue remodeling in affected organs. It is vital to systematically investigate sex disparities, possibly in different age groups, allergic diseases incidence, and their outcomes. When they are identified, it is necessary to elucidate their biological basis and understand if better outcomes could be obtained with sex-specific treatment modifications.⁸

There are different risk factors for developing allergic diseases in boys and girls. A longitudinal study found that obesity, together with rhinitis and current smoking were risk factors for developing asthma in girls, while the main risk factors for boys were reduced FEV1, seasonal allergic symptoms and a family history of asthma.⁹

To optimize clinical practice, it is necessary to understand, in addition to the molecular mechanisms and biomarkers, the phenotypes of allergic diseases, as well as the difference in their distribution between genders. This is recognized as an innovative element, as there is scientific evidence that men and women not only have distinct clinical manifestations for the same disease, but have different therapeutic responses. These can be influenced by biological (hormonal, organic) and socio-cultural factors (adherence to treatment, work, purchasing power).⁸

Men and women have different lifestyles, in terms of choosing specific professions, sports, intake of hormonal medications and quality of diet. Immune cells (lymphocytes, monocytes, eosinophils and mast cells) express hormone receptors and, therefore, may be highly influenced by endogenous and exogenous hormones, which fluctuate in women.¹

Longitudinal studies would be interesting to evaluate possible mechanisms underlying these differences in prevalence. Sex- and gender-specific evaluations beyond 14 years of age are scarce and further allergic multimorbidity studies in different populations, especially in adults, are necessary.³

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