

Immunoglobulin E Deficiency and Autoimmune Disease

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To the Editor:

In the article entitled “Relationship Between Immunoglobulin E Deficiency and Autoimmune Disease: The Paradigm of Primary Biliary Cholangitis” by Porto-Soto et al. [1], the authors discuss the relationship between autoimmune disease, especially primary biliary cholangitis (PBC), and IgE deficiency. I feel that a number of concerns must be addressed in order to better understand the research and the relationship between autoimmunity and IgE deficiency.

My first major concern is in Supplementary Table 1 [1], where a high IgE level was accepted as >100 kU/L. However, “normal” IgE levels are known to vary widely both in children and in adults from <2 to >200 kU/L [2]. For instance, the distribution of serum total IgE levels, even in nonatopic children at 5 years of age was found to be extremely wide-ranging in a study with the 3rd and 97th percentiles at 2.17 kU/L and 223.82 kU/L, respectively [3]. The total IgE level increases somewhat in parallel with age in older patients, and a value above 100 kU/L is considered high mostly for children under 6 years of age [3,4]. Moreover, the reference range for serum total IgE in young adults from 10 Western European nations [5] was the 95th percentile of the total IgE reference value (148 IU/mL in women, 169 IU/mL in men), which was lower than in studies conducted in Iran (227.6 in males and 312.3 in women) [6] and in Norway (302 kU/L for both sexes) [7]. These studies suggest that the value of >100 kU/L cannot be considered high for adults.

My second concern is with the authors’ statement that the selection of the control group patients was random and was not influenced by atopy or other diseases. It would be better if patients were selected based on the presence of diseases that increase IgE levels. The frequency of allergic/atopic diseases and of use of the medications prescribed (eg, antihistamines) in adulthood and related allergic reactions is high. One study showed an increase in total IgE levels from 6 years of age with the development of atopic sensitization [3]. Consequently, selection of patients is a key factor that may affect the statistical significance of the difference between the 2 groups (patients with PBC and the general adult population). It would also be better to question

comorbidities and medication use/treatment in the general adult population (the study control group).

Third, cigarette smoking should have been taken into account, and, if possible, smokers should not have been included in the control group or the general adult population [1]. Some literature data suggest that smoking leads directly or indirectly to an increase in serum IgE levels [8]. This increase can affect the total serum IgE level and, therefore, the statistical findings.

Less important but still worthy of mention is the reporting of high IgM levels (ie, that the most well-known humoral disorder is elevated serum IgM concentrations and that IgM concentrations were higher in the PBC patients) [1]. The presence of the hallmark of PBC in inborn errors of immunity (hyper-IgM syndrome) caused by mutations in the CD40 ligand gene is both interesting and valuable for our understanding of the immune pathogenesis of PBC [9]. Again, we wonder if any of the patients with PBC who have low IgE deficiency and high IgM level have hyper-IgM syndrome.

Familial IgE deficiency has also been described in the literature [10]. It would be interesting to know if there was familial IgE deficiency in this control group or in the study group and if a family history was taken and questioned. Once again, we can appreciate the importance of a clinical history in the diagnosis of diseases.

Our understanding of the pathogenesis of IgE deficiency would be aided by knowing whether these 2 allergic/immunologic disorders were present in the study group.

There is a typographic error in the second column on the first page ($P>.5$ in each case). This should be ($P>0.05$ in each case).

Finally, I would like to thank the authors for this elegant study. It will pave the way for new studies and increase awareness of (selective) IgE deficiency, an important disease that has received little attention.

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Conflicts of Interest

The author declares that he has no conflicts of interest.

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