LETTER TO THE EDITOR

Alpha-1 antitrypsin deficiency in Madeira Island: The first null variant and the contribution of deficient genotypes

Dear Editor,

Diagnosis of alpha-1 antitrypsin deficiency (AATD) has improved considerably due to an increasing awareness about the disease and the publication of evidence-based international diagnostic and management guidelines in the last 15 years.1,2

Patients with AATD are at increased risk of developing lung disease, like panlobular basal emphysema, chronic obstructive pulmonary disease (COPD) and bronchiectasis.1,3 On the other hand, liver fibrosis, steatosis, cirrhosis and hepatocarcinoma had also been described in AATD patients.1,4 Pi*ZZ is the most frequent genotype associated with both pulmonary and hepatic manifestations of AATD,1,3 affecting approximately 1/3500 to 1/6000 individuals of European descent.1 Other rare deficiency variants were described worldwide, like M_Maltonia (rs779982338: p.Phe76del) and several null variants (Q0), the latter being unable to produce AAT and to form polymers in the liver.1,4

Madeira Island has a population of 250,000 people and has been described as having one of the highest prevalence of patients with AATD.4 Here, we report the frequency of AATD patients on Madeira Island, tested with a clinical suspicion for the disease and the publication of evidence-based international diagnostic and management guidelines in the last 15 years.1,2

We observed that the prevalence of certain alleles has been increasing in Madeira population, like Pi*Z and Pi*S. Previously, in a paper focused on this subject, 8 patients with Pi*MZ, 6 with Pi*SS, 2 with Pi*SZ and no Pi*ZZ patients were reported.6 Nowadays, we have identified an increase in the frequency of those genotypes: 62, 11, 39 and 38 patients, respectively. In addition, rare deficiency and null

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variants were detected accounting for a significant percentage of the patients followed in our hospital, namely M Malton (n = 60; 25.6%) and Q0 Santana (n = 3; 1.3%).

AATDs diagnosis is increasing in Madeira Island and severe disease is seen in many patients, due to the high prevalence of Pi*Z and Pi*M Malton. Recently we discovered a null variant specific of this region, Q0 Santana. Even in non-smokers, the presence of these alleles is responsible for remarkable lung parenchyma alterations and impaired lung function.

**Conflicts of interest**

The authors declare no conflict of interests.

**References**


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