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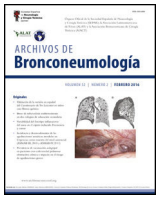

Letter to the Director

## Alpha-1 Antitrypsin Deficiency Severe and No Severe. Is It Benefit or Risk?

*To the Director,*

We have read with interest the article published by Riley et al. titled "Labelling Alpha-1 antitrypsin deficiency in the medical record – A call to action",[1] and we would like to make some considerations in this regard. The first is that the authors classify subjects diagnosed with alpha-1 antitrypsin deficiency (AATD) into severe and non-severe according to 2 criteria: having a *Pi*ZZ* genotype or serum levels of alpha-1 antitrypsin (AAT) ≤ 57 mg/dL (≤11 μmol/L). From our point of view, this classification brings more risks than benefits. It considers severe to healthy patients, or on the contrary it considers not serious deficiency to patients with AATD-related disease and finally one must take into account the psychological considerations of the patients. Since we know that AATD is a genetic condition (and not a disease), which predisposes those who carry it to develop respiratory pathology in the form of emphysema and/or liver involvement in the form of cirrhosis mainly.[2] This implies that not all AATD individuals will develop diseases, regardless of their genotypes, even if their plasmatic AAT levels are very low.[3] Therefore, subjects with very deficient genotypes but who are healthy would be classified as serious when in reality they are not, confusing the responsible physicians and the patients themselves. The same would occur in those subjects with blood levels of AAT > 57 mg/dL and who had developed pathology (e.g. *Pi*SZ*, or heterozygotes of rare variants).

Secondly, it has caught our attention that in patients categorized as severe AATD, despite having alterations in respiratory function tests (very low $FEV_1$ and DLCO and indirectly indicative of emphysema-type COPD), less than half, were on augmentation treatment. That expert guidelines and consensus recommend starting treatment in this type of subject as soon as possible, because intravenous augmentation therapy reduces the progression of emphysema and therefore its morbidity and mortality.[4] However, in a patient with the *Pi*MZ* genotype if he was on treatment. If we review the indications according to the latest European Guide for the Diagnosis and Treatment of AATD, the *Pi*MZ* genotypes are excluded for it, because there is no evidence to support efficacy of AAT augmentation therapy in patients with genotype like *Pi*SZ*, *Pi*MZ* or current smokers of any genotype.[4]

The authors use the value of ≤57 mg/dL (≤11 μmol/L) serum levels of alpha-1 antitrypsin (AAT) as the limit of the protective threshold, however, in a review by Franciosi et al.,[5] they recommend not using this value, because there is no evidence that this "apparently protective limit" is adequate in the reviewed literature, and that even using it to make decisions about treatments or other actions may not be adequate and have consequences for patients.

In our opinion, it is clear that among patients with AATD, we must distinguish between those who present significant involvement, either pulmonary or hepatic, based on clinical and functional criteria, from those who have not developed disease and are therefore healthy, because it is a clear benefit for patients. We believe that this type of genetic predisposition should be managed by experts with experience in this type of patients, because the clinical variability of these patients is very wide and a classification as suggested by Riley and Lescano, with severe and non-severe AATD can lead to more risk as we specified above.

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## Conflict of interest

The author declares have no conflicts of interest related directly or indirectly to the contents of the manuscript.

## References

1. Riley L, Lascano J. Labelling Alpha-1 antitrypsin deficiency in the medical record – a call to action. Respir Med. 2022;193:106749, http://dx.doi.org/10.1016/j.rmed.2022.106749.
2. Matamala N, Lara B, Gómez-Mariano G, Martínez S, Vázquez-Domínguez I, Otero-Sobrino Á, et al. miR-320c regulates SERPINA1 expression and is induced in patients with pulmonary disease. Arch Bronconeumol. 2020, http://dx.doi.org/10.1016/j.arbres.2020.03.006. S0300-2896(20)30084-3.
3. Blanco I, Lara B. Alpha-1 antitrypsin deficiency: pathophysiology, related diseases and treatment. Respira-Spanish Lung Foundation-SEPAR, editor. Barcelona; 2016.
4. Miravitlles M, Dirksen A, Ferrarotti I, Koblizek V, Lange P, Mahadeva R, et al. European Respiratory Society statement: diagnosis and treatment of pulmonary disease in α1-antitrypsin deficiency. Eur Respir J. 2017;50:1700610, http://dx.doi.org/10.1183/13993003.00610-2017.

https://doi.org/10.1016/j.arbres.2022.05.012

5. Franciosi AN, Fraughen D, Carroll TP, McElvaney NG. Alpha-1 antitrypsin deficiency: clarifying the role of the putative protective threshold. Eur Respir J. 2022;59:2101410, http://dx.doi.org/10.1183/13993003.01410-2021.

José María Hernández Pérez*, Claudia Vivian López Charry

*Department of Neumology, Universitary Hospital Nuestra Señora de Candelaria, Carretera del Rosario 145, 38010 Santa Cruz de Tenerife, Spain*

Corresponding author.
*E-mail address:* jmherper@hotmail.com (J.M. Hernández Pérez).