8.21 The Irish Null Cohort: A Case Series

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Background: Alpha-1 antitrypsin deficiency (AATD) is a genetic condition caused by a spectrum of SERPINA1 gene mutations, resulting in insufficient levels of a protective protein, alpha1 antitrypsin (AAT). The degree of AAT deficiency confers varying risks of emphysema and liver disease[1]. The Null genotype (Q0) refers to a subgroup of rare SERPINA1 mutations, which cause complete absence of AAT protein production and confer the highest risk of pulmonary damage1.

Case Series: This novel case series examines the clinical presentations and disease trajectories of an Irish cohort of patients with rare null phenotypes. Considering the autosomal co-dominant nature of inheritance of AATD, we compared the heterozygotic phenotypes M-Null, Z-Null and the exceedingly rare Null-Null. This cohort provides a significant diagnostic challenge, present earlier with higher symptom burden, deteriorate rapidly with pathological stressors, and struggle to recover lung function post insults. We also demonstrate the geographical prevalence of several null mutations, including Q0porto, Q0dublin and Q0bolton. **Conclusions**: Early recognition of rare phenotypes is key to timely intervention. Accurate genetic diagnosis depends on increased awareness, utilisation of multiple collaborative diagnostic techniques and expert interpretation[2]. While exciting novel therapies loom on the horizon, hinting at the dawn of precision medicine, the absence of government funding of existing treatments (which have been shown to have significant benefit in this niche population[3]) remains a significant barrier in Ireland.

References:

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