Alpha1 MZ Foundation - Information & Research

News & Research Update

Oct 5, 2024

Dear Subscribers,

Last week, we had the privilege of attending a highly significant and impeccably organized Alpha1 day in the Netherlands. Thank you LUMC and the organizers!! These days are of the utmost importance for patients in their search for answers and treatment.

Did you know that only in the Netherlands, there are more than half a million persons affected by the Z mutation without knowing it, and that a big part of that group is suffering unnecessarily and costing our society a lot of money? (This is based on our research out of DNA testing in the Netherlands, which shows that 3.2% of the population in the Netherlands has at least one Z mutation)

While we were there, the ZZs asked quite a few questions about their sometimes struggling MZ children, which clearly shows that besides looking at the more obvious and well-known easy-to-diagnose Lung and Liver morbidities, there is still a lot more research and attention required to address the more challenging-to-diagnose morbidities described in the more recent research papers.

Let me summarize a few of these more challenging morbidities to diagnose:

1. Immune Dysregulation:
Alpha-1 antitrypsin (AAT) has anti-inflammatory properties that help regulate immune responses, particularly by inhibiting neutrophil elastase, a protease involved in inflammation. In individuals with lower levels of AAT it can lead to uncontrolled immune responses. This can manifest as excessive inflammation and tissue damage, particularly in the lungs but also in other organs.

2. Autoimmune Diseases:
There is a link between AAT deficiency and an increased risk of autoimmune disorders due to the dysregulation of the immune system. This includes potential connections to conditions like vasculitis and rheumatoid arthritis, where the immune system attacks connective tissues.

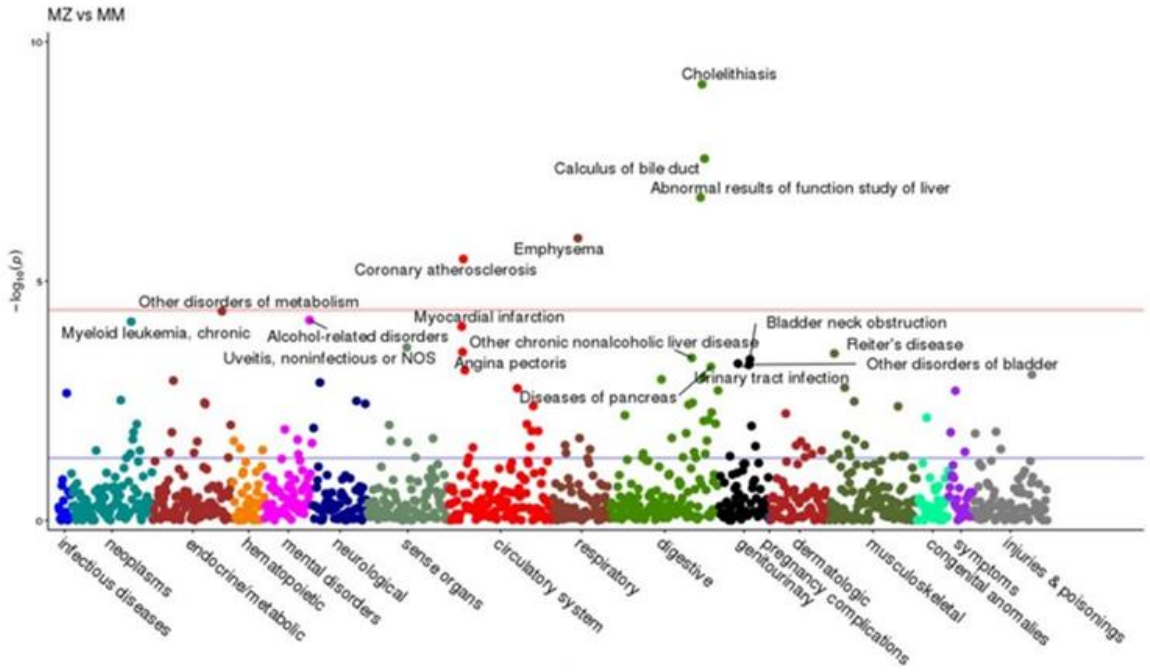
3. Impact on Connective Tissue:
AAT's role in protecting tissues from enzymatic degradation extends to connective tissues. In individuals with a reduced AAT level, this can result in an imbalance between proteases and their inhibitors, which can lead to the degradation of elastic fibers and collagen. This may contribute to conditions like panniculitis, a rare inflammatory condition affecting subcutaneous fat, and connective tissue fragility.

Structural Weakness: The deficiency in AAT protection can weaken connective tissues, particularly in the lungs, leading to emphysema but also impacting joints, tendons, and skin elasticity.

4. Impact on the biliary tract (Specific for MZ)
Below, I have added a diagram for the MZs and the ZZs with MZ children that clearly shows the impact of the MZ combination, specifically on liver-induced biliary tract morbidities.
This is based on a paper from 2020 by “Nakanishi T, Forgetta V, Handa T, et al. The Undiagnosed Disease Burden Associated with Alpha-1 Antitrypsin Deficiency Genotypes”
This is a UK Biobank study with 458,164 participants and 16,983 MZs, which clearly indicates the liver-induced biliary tract issues unique to MZs.

And don’t forget that 1 out of 15 MZs face Cholestasis during pregnancy and need proper guidance during their pregnancy to avoid serious issues during their pregnancy for both mother and child. (3x higher than MM)
The impact of the biliary tract issues should not be underestimated because it leads to malnutrition and essential vitamin and mineral deficiencies, which in turn leads to serious 2e and 3e order morbidities.

In conclusion, there is still much work ahead of us regarding research, education, and awareness for both patients and medical professionals. Think about the General Practitioner you visit who is not even aware that more than 3% of their patients are affected and the fact that they did not receive proper education/information about this condition based on the latest research.



And, like always, enjoy the ride !!

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