Alpha1 MZ Foundation - Information & Research

News & Research Update

Jul 27, 2024

Dear Subscribers,

Because the number of subscribers has grown rapidly during the last few months, we want to summarize the extensive disease burden among the Alpha1 MZ population. You can find more details and related research papers on our website. www.alpha1mz.org.

It is also important to consider that it becomes increasingly clear that the disease burden of the MZ genotype is different/additional compared to the known disease burden of the ZZ genotype.
Enjoy reading, especially the relatively unknown disease burdens at the end of this update.

1. Airways / Lungs

In simple terms, Alpha 1 Antitrypsin protects the lungs from inflammation and damage caused by inhaling irritants such as tobacco smoke and/or other air pollution particles. This means that a lower AAT level gives you less "protection" for your lungs.

The lower the AAT level, the lower the "protection." This means that depending on your lifestyle and environment, the *probability* of developing lung emphysema during your life is very high when you are a ZZ, still high when you are an SZ, and moderate when you are an MZ. Of course, it all depends on the air quality and exposure to cigarette smoke, dust, etc.
As an example, some MZs had a lung transplant, and some ZZs are still fine at the same age. It's all depending on the environment you live in.

A lower level of AAT is also related to Bronchiectasis.

2. Liver

Mutations in the SERPINA1 gene, which encodes the liver's alpha-1 antitrypsin (AAT) protein, cause our disease burden. In an Alpha 1 MZ individual, the "M" portion is correctly formed and secreted into the bloodstream; however, the "Z" portion of the protein is not correctly formed and cannot leave the liver cell. It is stuck and causes a lower Alpha1 Antitrypsin protein level in your blood and continuous liver stress, which may lead to liver fibrosis and cirrhosis depending on other genes that determine the autophagy speed. Please note that the "Z" portion, which gets stuck in your liver, also influences the liver's capacity to perform more than 500 other vital liver functions for your body.

3. Fatty liver

We see that most, if not all, MZs are diagnosed with fatty livers. We understand that Western food and lifestyle do not help the MZ liver. However, the root cause of the high prevalence of fatty livers is continued liver stress, particularly in the Endoplasmic Reticulum of the Hepatocyte, which is

responsible for processing the fatty acids. (A liver-friendly diet is recommended for all MZs)

4. Biliary tract

Several research studies proved an increased risk of Biliary Tract issues for patients with genotype MZ, and this correlates with our observations within the Alpha 1 MZ group, which may also explain the reported intermittent pain in the liver area.
These issues worsen as one ages because the liver loses more capacity through aging and continued liver stress. The continued liver stress may result in lower bile availability, which causes biliary tract issues. This has a negative effect on the microbiota composition in the small intestines (SIBO), which, in turn, leads to vitamin and mineral malabsorption and related vitamin and mineral deficiencies. The main symptoms are gastrointestinal problems such as abdominal pain, bloating, gas, diarrhea, and constipation.

The fact that MZs are more prone to develop biliary tract issues is also confirmed in research showing that 1 out of 15 MZ women develop biliary tract issues during pregnancy, resulting in serious complications for mother and child.

5. Vitamin and mineral deficiencies (examples)

Vitamin B12; This is the first vitamin typically affected. Vit B12 is secreted by the liver together with Bile Acid, and because of biliary tract issues, Vitamin B12 is also affected, which in turn leads to very serious mental and physical issues.

Vitamin D: Because of calcium malabsorption, your body will use more Vit D compared to a normal person, which leads to a Vitamin D deficiency. (a change to a more healthy diet with less sugar and more minerals helps)
Important note: Be very careful with supplementing vitamin D3. Vitamin D3 needs to be converted in the liver to vitamin D25, and because of the lower capacity of the MZ liver, high doses may cause liver damage, as some MZs have experienced.

6. Neurological issues

Because of vitamin B12 deficiencies, neurological issues that affect the brain and nervous system will develop over time within the Alpha1 MZ group and can be very serious, from dementia, delirium, cerebellar ataxia, psychosis, neuropathy, and mood disorders, even leading to ending up in a wheelchair. (A preliminary study showed 7 out of 10 had a B12 deficiency. Statistical studies are in preparation)

7. Connective Tissue & Aneurysm

Alpha1 Antitrypsin inhibits elastase, which is important in remodeling and repairing connective tissue. Elastase production increases with inflammation, and an individual with an MZ genotype will have increased degradation of the connective tissue matrix, leading to decreased joint stability."
In patients with AATD, the lack of Neutrophil Elastase inhibition and overactivity of proteases can degrade elastin and connective tissues, leading to a loss of elasticity in vessel walls, increased stiffness, and reduced distensibility. This can result in aortic wall weakening and aortic distention"

There is an abundance of evidence reporting the protective role of AAT in preserving arterial wall integrity. Within our MZ group, it was reported that many passed away because of an aortic aneurysm. (When you are getting older, check your aorta regularly for aneurysm)

8. Background Inflammation

Research showed that 25% of the Alpha1 MZ group showed a high background inflammation level compared to healthy persons, which clearly indicates the amount of MZ affected.

9. Immune regulatory and Auto-immune

Research showed that AAT has an immunoregulatory and anti-inflammatory role, and a deficiency may cause autoimmune issues and a lowered immune system (Lymphocytes / T cells)
Many of the MZs in our group are affected by a lower-than-normal immune response. (More research is required.)

10. Skin diseases

Alpha-1 Antitrypsin Deficiency can cause panniculitis, a skin condition resulting in painful, raised red bumps on the skin. Our members also often report eczema.

11. Autism

A significantly high number of autistic family members have lower than normal serum levels of AAT when compared to controls. Autistic children with regressive onset had significantly lower levels of AAT compared to controls, and a significant number of autistic children with low serum AAT also had hyperbilirubinemia, gastrointestinal disease, and respiratory problems. The researchers also found that a significantly high number of these individuals had the PiMZ genotype and correspondingly low levels of serum alpha-1 antitrypsin.

And like always, enjoy the ride !!

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