

Alpha 1 Antitrypsin MZ Information & Research

News & Research Update

Jun 29, 2024

Dear Subscribers,

Last week I met another MZ at an event, and she asked me if I knew what causes the pain on the right side around the lower ribs (the right hypochondriac). Because this intermittent pain was also reported by 9 out of 10 MZ's which participated in our preliminary study, it's time to spend some time on this subject and explain what is causing this "pain".

First of all, most MZ's report that it is an intermittent "pain". The amount of pain varies from something like itching under the ribs to real noticeable pain. For most, it may start like some itching at age 40-45, and it gets worse (uncomfortable sometimes) when you are getting older, let's say 60+, but this is different from person to person.

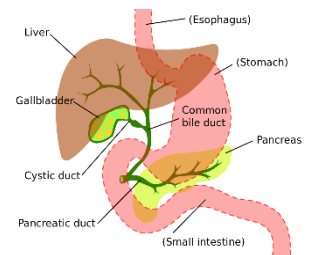
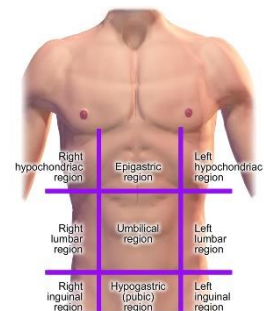
As you can see on the picture on the right side, the organs at that location are mainly the liver, the gall bladder and parts of the biliary tract. We can rule out the liver because the liver does not contain nerve fibers that sense pain. However, there are pain fibers in the liver's capsule, a thin layer of tissue that surrounds the liver. So when the liver is growing in size it may cause a pain sensation, but this scenario is not likely..

Then we get to the gall bladder, which is roughly at the same location, which is a much more likely candidate, because MZ's have a known high prevalence of biliary tract and gall bladder issues which are unique to Alpha1 MZ, according to the UK Biobank report.

First, a short description of how the "bile system" works.

When the liver cells secrete bile, it is collected by a system of small ducts that flow from the liver through the right and left hepatic ducts, and these ducts ultimately drain into the common hepatic duct. The common hepatic duct then joins with the cystic duct from the gallbladder to form the common bile duct. This runs from the liver to the duodenum (the first section of the small intestine). However, not all bile runs directly into the duodenum. About 50% of the bile produced by the liver is first stored in the gallbladder. This is a pear-shaped organ located directly below the liver. Then, when food is eaten, the gallbladder contracts and releases stored bile into the duodenum to break down the fats in your food.

Because of the high prevalence of gall bladder / biliary tract issues among Alpha1 MZ's, as reported by the UK biobank study, and this in combination with the high prevalence of MZ's which are reporting an intermittent pain in the right hypochondriac, it is very likely that this pain is caused by



the gall bladder or parts of the biliary tract in that area.

Secondly, let's talk about the root cause of the gall bladder / biliary tract issues of the MZ's. The cause of this is hypothesized to be a reduced secretion of bile acid induced by the Hepatocyte Endoplasmic stress in the liver, which in case of an MZ involves all liver lobule zones including the pericentral zone, where most of the bile acid is produced. (This is supported by research papers)

It is also known that a reduced bile acid secretion by the liver causes gall bladder issues which the MZ's are experiencing. And of course the reported 7% prevalence of cholestasis during pregnancy under MZ's is also a clear indicator in that direction. (Cholestasis means a reduction or stoppage of bile flow)

In conclusion, the "pain" in the right hypochondriac you may be experiencing as an Alpha1 MZ seems to be quite common, especially for older MZ's where the liver has lost 30-40% capacity due to aging, and as such secretes less bile acid, which has an impact on the gall bladder "health".

It is also important to understand that most of the bile (salts) are reabsorbed, and that the remaining bile is excreted from the body in the feces, and this is what gives feces its **dark brown color**. A reduction / shortage of bile may lead to a **light colored** stool. Something to be aware of and check on a regular basis.

And like always, enjoy the ride !!

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