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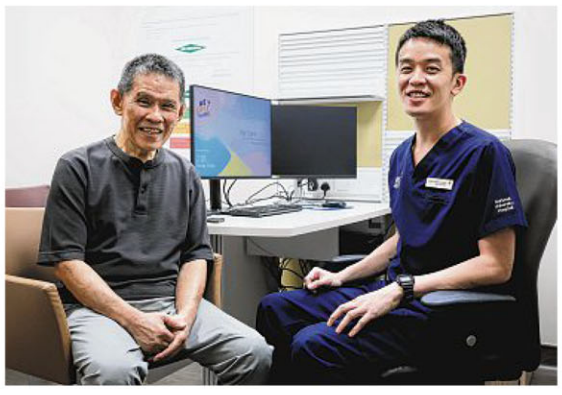

Adjunct Associate Professor Daniel Huang (right) of the NUH Department of Medicine's division of gastroenterology and hepatology with his patient, Mr Foo Say Nong, on May 25. ST PHOTO: GAVIN FOO

# Fatty liver genes combined with diabetes, obesity raise liver cancer risk: Study

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Researchers in Singapore have found that a specific genetic change that results in fatty liver, when combined with metabolic conditions like diabetes and obesity, is linked to a higher risk of liver cancer. Genetic risk does not act in isolation.

The researchers also found that men with what is commonly known as a "beer gut" face a higher risk – of up to nine times – of having the most common type of primary liver cancer, called hepatocellular carcinoma. "Beer gut" refers to a build-up of visceral fat around the internal organs, especially the liver.

The study was published in May in Alimentary Pharmacology and Therapeutics, a leading international journal in gastroenterology. It is among the first large-scale prospective analyses in Asia to demonstrate a clear relationship between the genetic variant of fatty liver and liver cancer risk.

Previously, individuals deemed to be at risk of liver cancer were tested for either fatty liver or metabolic conditions, but not together, said the study's principal investigator, Adjunct Associate Professor Daniel Huang.

"Our findings show that diabetes and obesity effectively 'stack' on top of genetic susceptibility to further increase liver cancer risk," Prof Huang, who is from the division of gastroenterology and hepatology of the National University Hospital (NUH) Department of Medicine, told The Straits Times.

"This highlights the importance of considering genetic factors together with information from routine medical checks, such as diabetes, high blood pressure, high cholesterol and being overweight, rather than viewing them separately."

Also, genetic association appeared more prominent among individuals without chronic hepatitis B, underscoring its relevance as liver cancer increasingly arises from non-viral causes, such as fatty liver disease and metabolic conditions, he added.

Genetic testing is not currently part of routine liver cancer screening in Singapore. But the findings of the recent study suggest it may be beneficial to combine genetic information with readily available clinical data to support more targeted, risk-based screening strategies in the future.

"This will help identify individuals who may benefit from closer monitoring, including those who may not fall within traditional high-risk groups," said Prof Huang, who is also chair of the Hepato-Pancreato-Biliary Cancer Programme at the National University Cancer Institute, Singapore (NCIS).

The research was carried out by scientists from NUH; the NUS Yong Loo Lin School of Medicine; NCIS; and the A*STAR Genome Institute of Singapore.

Its findings come from a large, population-based study involving nearly 25,000 participants from the Singapore Chinese Health Study, a cohort established since 1993 for research on cancer and other chronic diseases of importance in Singapore and worldwide.

According to the Singapore Cancer Registry Annual Report of 2023, liver cancer was among the three leading contributors to cancer deaths for males between 2019 and 2023.

Liver cancer is often asymptomatic in its early stages, and many patients are diagnosed only when the disease is advanced, limiting treatment options.

With the rise of fatty liver disease as a major cause of liver cancer, these findings highlight how clinical factors – including gender, diabetes and obesity – can meaningfully influence risk when combined with genetic susceptibility.

Prof Huang has launched a new follow-up study looking at both the genetics of fatty liver and metabolic conditions. He aims to recruit about 200 liver cancer patients and their families for the study.

About 170 patients have stepped forward so far. One of them is retiree Foo Say Nong, 74, who was diagnosed with liver cancer in 2010 at another hospital and then again in 2018 at NUH.

"I didn't have any symptoms or pain at all. Without regular follow-ups, it could easily have gone unnoticed," Mr Foo said, adding that he underwent minimally invasive surgery at NUH and had the tumour "successfully removed".

When he volunteered to participate in the research study in 2025, a scan performed as part of the research detected a new, unrelated liver tumour in the early stage.

Mr Foo underwent image-guided ablation and is currently in remission.

"I found out how important this research is in improving early detection. I encouraged my sister and my son to take part (in the study). I also advised my friends with a big tummy to also come forward, saying it would be good for them."

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