Higher Risk of Liver Cancer in People with NAFLD Linked to High Blood Iron Levels

Research has shown that elevated levels of iron in the blood from hereditary hemochromatosis can raise the risk of HCC.

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New research has found that patients with nonalcoholic fatty liver disease (NAFLD) who have high blood iron levels are at an elevated risk to develop the most common type of liver cancer, hepatocellular carcinoma (HCC). Researchers at the University of Pittsburgh [presented] their findings this week at The Liver Meeting Digital Experience, held by the American Association for the Study of Liver Diseases.

Research has shown that elevated levels of iron in the blood from hereditary hemochromatosis, a disorder that causes the body to absorb too much iron, can raise the risk of HCC. However, there is little data on patients with NAFLD. HCC is a common liver condition that is estimated to affect about 25 percent of adults worldwide.

“NAFLD may contribute to the rising incidence of HCC in the U.S. However, only a small fraction of NAFLD patients eventually develop HCC. The liver is the primary reservoir of body iron. The iron overload can cause hepatotoxicity and liver damage,” said Jian-Min Yuan, MD, PhD, the senior author of the new study, the chair of cancer prevention at UPMC Hillman Cancer Center and a professor of epidemiology at the University of Pittsburgh School of Medicine. “A direct link between serum iron level and HCC risk would support a harmful role of iron elevation on HCC development in NAFLD patients.”

The researchers analyzed how elevated levels of any one of the four iron biomarkers was associated with HCC, with adjustments for age, sex, race, body mass index, type 2 diabetes history and smoking tobacco. They found that, compared with those who do not develop cancer, NALFD patients who developed HCC:

- Tend to be older, male and past or present smokers.
- Are more likely to have a history of type 2 diabetes and hypertension but lower levels of lipids.

The researchers also discovered that when it comes to links between HCC risk and iron levels in NAFLD patients:

- An elevated level of serum iron, or more than 175 mcg/dL, is associated with more than double the HCC risk of normal serum iron levels.
- A higher level of transferrin saturation, or more than 35%, was associated with a twofold increase in HCC risk compared with a normal transferrin saturation of 25%to 35%.
- There were no statistically significant associations between HCC risk and total ironbinding capacity.
- Elevated serum ferritin levels were not significantly associated with an increased cancer risk.

“Since HCC develops in only a small percentage of NAFLD patients, our findings — if confirmed in larger, prospective studies — may help identify patients at increased risk of developing HCC. Those patients could then be targeted for more intensive surveillance,” Yuan said. “However, since serum iron levels change constantly in response to physiologic needs, more research is needed to understand the clinical implications of persistence and magnitude of serum iron elevation, as well as the lack of association of ferritin levels with HCC risk in NAFLD patients.”

Yuan and his research team identified 47,165 patients ages 40–89 who were diagnosed with NAFLD between 2004 and 2018 using electronic health records at the University of Pittsburgh Medical Center. There were 18,569 patients who had at least one of the iron-related blood test results needed for the analysis: serum iron, transferrin saturation, total iron binding capacity or serum ferritin. After an average of 4.3 years of follow-up, 224 patients developed HCC.

Dr. Yuan’s poster entitled Elevated Serum Iron Levels Are Associated with Increased Risk of Hepatocellular Carcinoma Incidence Among Patients with Nonalcoholic Fatty Liver Disease (1048) can be viewed at The Liver Meeting Digital Experience, Nov. 12–15, 2021. The corresponding abstract can be found in the journal HEPATOLOGY.

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