Scientists identify likely predictors of hepatitis C severity: viral evolution and host protein levels

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(Medical Xpress) -- Scientists at the National Institutes of Health have identified several factors in people infected with the hepatitis C virus that may predict whether the unusually rapid progression of disease from initial infection to severe liver conditions, such as cirrhosis, will occur. Knowing whether a patient's condition is likely to deteriorate quickly could help physicians decide on the best course of treatment.

The study was conducted by an international team of researchers led by Patrizia Farci, M.D., chief of the Hepatic Pathogenesis Section in the Laboratory of Infectious Diseases at the National Institute of Allergy and Infectious Diseases (NIAID), part of NIH; and Harvey Alter, M.D., chief of clinical studies and associate director of research in the Department of Transfusion Medicine at the NIH Clinical Center. Their findings appeared online July 23 in the Proceedings of the National Academy of Sciences.

“Treatment for hepatitis C is often expensive and poorly tolerated,” said NIAID Director Anthony S. Fauci, M.D. “Tools that would enable physicians to better predict the course of disease progression in hepatitis C patients would help guide treatment decisions. This small study is a potentially important step in developing such tools.”

Symptoms of acute infection with the hepatitis C virus, one of five viruses that cause acute and chronic hepatitis, include fatigue, jaundice

and loss of appetite. Between 70 and 80 percent of people infected with the hepatitis C virus develop chronic infection, which over a patient's lifetime may result in severe liver diseases, such as liver cancer and cirrhosis. The World Health Organization estimates that 130 million to 170 million people live with chronic hepatitis C. Approximately 2.7 million to 3.9 million of those people live in the United States, according to the Centers for Disease Control and Prevention.

After a person is infected with hepatitis C, the virus evolves and circulates in the body in the form of several closely related strains, which allows it to adapt to drug treatments and avoid elimination. Some genetic differences between these strains result in changes to the proteins they encode, while others do not.

“A major mystery in the study of hepatitis C is that the disease course can be highly variable,” explained lead researcher Dr. Farci. “Some patients show no symptoms for decades and eventually die of other causes. Other patients rapidly develop cirrhosis and liver cancer, leading to liver-related death in less than ten years.”

Studies have found that having a weakened immune system — for example, as the result of HIV infection or organ transplantation — can exacerbate hepatitis C-related disease. But this does not fully explain which hepatitis C patients will ultimately experience a more rapid health decline. At present, there is no way to predict how the disease will progress in any given patient.

The new study involved samples collected from six patients who were infected with hepatitis C via contaminated blood transfusions in the 1970s, before the virus was identified. Blood donations have been routinely tested for hepatitis C since 1990. The patients’ symptoms and clinical outcomes were closely followed from the day they received the transfusion for up to 30 years, and ranged from mild and stable chronic

hepatitis C to rapid disease progression and death.

Dr. Alter and his Clinical Center colleagues periodically collected blood serum samples from each of the six patients. Dr. Farci and her NIAID colleagues used up to 17 of these archived samples per patient to obtain and analyze a total of 1,876 genetic sequences of the hepatitis C virus. The researchers used the genetic sequences to reconstruct the evolution of two particular hepatitis C genes, E1 and E2, and the research team analyzed the types of genetic changes that took place in order to understand their relationship with disease progression. They also studied the levels of 39 blood serum proteins during the acute and chronic phases of disease.

“We thoroughly characterized the biological changes that occurred in these patients, and we discovered that patients who developed rapidly progressive disease had specific changes in their blood that were detectable since the early acute phase of infection,” said Dr. Farci. Patients with rapid disease progression had significantly higher levels of a protein known as MCP-1, which is believed to play a major role in the development of liver fibrosis, and, eventually, cirrhosis. Moreover, in these patients, the genetic changes in the virus as it evolved over time were less likely to result in changes to the virus proteins.

The researchers say genetic and blood serum markers may one day enable physicians to identify hepatitis C patients at risk for rapid progression and to use this information to adjust their treatment. Additional markers may exist, Dr. Farci explained. The research team is working to increase the sample size by doing similar analyses on the remaining stored samples.

“Now that we know what to look for, we believe it is extremely important to extend our observation to a larger number of patients,” Dr. Farci said.