

Natural History

After acute infection, 15%-25% of persons appear to resolve their infection without sequelae as defined by the sustained absence of HCV RNA in serum and normalization of ALT levels. Chronic HCV infection develops in most persons (75%-85%) with persistent or fluctuating ALT elevations indicating active liver disease developing in 60%-70% of chronically infected persons. In the remaining 30%-40% of chronically infected persons, ALT levels are normal. No clinical or epidemiologic features among patients with acute infection have been found to be predictive of either persistent infection or chronic liver disease. Moreover, various ALT patterns have been observed in these patients during follow-up, and patients might have prolonged periods (≥ 12 months) of normal ALT activity even though they have histologic-confirmed chronic hepatitis. Thus, a single ALT determination cannot be used to exclude ongoing hepatic injury, and long-term follow-up of patients with HCV infection is required to determine their clinical outcome or prognosis.

The course of chronic liver disease is usually insidious, progressing at a slow rate without symptoms or physical signs in the majority of patients during the first two or more decades after infection. Frequently, chronic hepatitis C is not recognized until asymptomatic individuals are identified as HCV-positive during blood donor screening, or elevated ALT levels are detected during routine physical examinations. Most studies have reported that cirrhosis develops in 10%-20% of persons with chronic hepatitis C over a period of 20-30 years, and HCC in 1%-5%, with striking geographic variations in rates of this disease. However, when cirrhosis is established, the rate of development of HCC might be as high as 1%-4% per year. In contrast, a study of > 200 women 17 years after they received HCV-contaminated RH factor IG reported that only 2.4% had evidence of cirrhosis and none had died. Thus, longer term follow-up studies are needed to assess the lifetime consequences of chronic hepatitis C, particularly among those who acquired their infection at young ages.

Although factors predicting severity of liver disease have not been well defined, recent data indicate that increased alcohol intake, being aged >40 years at infection, and being male are associated with more severe liver disease. In particular, among persons with alcoholic liver disease and HCV infection, liver disease progresses more rapidly; among those with cirrhosis, a higher risk for development of HCC exists. Furthermore, even intake of moderate amounts (>10 grams/day) of alcohol in patients with chronic hepatitis C might enhance disease progression. More severe liver injury observed in persons with alcoholic liver disease and HCV infection possibly is attributable to alcohol-induced enhancement of viral replication or increased susceptibility of cells to viral injury. In addition, persons who have chronic liver disease are at increased risk for fulminant hepatitis A.

Extrahepatic manifestations of chronic HCV infection are considered to be of immunologic origin, and include cryoglobulinemia, membranoproliferative glomerulonephritis, and porphyria cutanea tarda. Other extrahepatic conditions have been reported, but definitive associations of these conditions with HCV infection have not been established. These include seronegative arthritis, Sjögren syndrome, autoimmune thyroiditis, lichen planus, Mooren corneal ulcers, idiopathic pulmonary fibrosis (Hamman-Rich syndrome), polyarteritis nodosa, aplastic anemia, and B-cell lymphomas.

Source: CDC