Studies reveal hepatitis C virus carriers experience substantial increase in mortality

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Hepatitis C virus (HCV) is a blood-borne disease that causes inflammation of the liver and to which there is currently no vaccine available. The World Health Organization (WHO) estimates that 3% of the world's population, approximately 170 million people, are infected with HCV and it is a leading cause of liver cirrhosis, end stage liver disease, hepatocellular carcinoma (HCC) and liver transplantation.

Researchers at Kagoshima University Graduate School of Medical and Dental Sciences concluded a 10-year study in Japan (where there is a greater incidence of HCV) and found the overall mortality rate was higher in HCV carriers. A second study, led by Dr. Adeel Butt from the University of Pittsburgh School of Medicine, looked at the effect of HCV on survival rate and also confirmed individuals infected with HCV had much higher death rates. Both findings appear in the August issue of *Hepatology*, a journal published by John Wiley & Sons on behalf of the American Association for the Study of Liver Diseases.

The Kagoshima research team, led by Hirofumi Uto, studied 1,125 individuals with the HCV antibody from 1995 through the end of 2005 or to their earlier death. Of the total, 758 (67.4%) had detectable HCV core antigen (HCVcAg) or HCV Ribonucleic Acid (HCV RNA) and were classified as carriers meaning the patients were viremic. The 367 (32.6%) individuals who had a prior HCV infection, but tested negative for both HCVcAg and HCV RNA were considered non-carriers or non-viremic.

According to the study, a total of 231 deaths occurred in the subjects over an average of 8.2 years of follow-up with 176 deaths in the HCV carrier group and 55 of the non-carriers. Using death certificates, researchers classified the deaths into 7 categories: hepatocellular carcinoma, liver disease (excluding HCC), neoplasms (excluding HCC), stroke, heart disease, pulmonary disease (excluding lung cancer) and unknown/other causes.

"Adjusting for age and gender," researchers concluded, "the elevated mortality rate among the subjects with HCV viremia was due to a much higher occurrence of liver-related deaths, but was not significantly associated with death from other malignancies such as stroke, heart disease, or pulmonary disease." The study notes that the higher overall mortality rate is explained by the higher rate of liver-related deaths from HCC and non-HCC with a cumulative risk of death of 28.0% for carriers, compared to 17.8% for non-carriers (based on Kaplan-Meier estimates).

Additionally, researchers observed that high HCVcAg levels were predictive of liver-related deaths, including HCC, in the HCV carriers. "Monitoring HCV load and ALT level in HCV carriers may be important for identifying those individuals at increased risk for HCC or other liver disease, particularly among older carriers who are less likely to respond to HCV treatment," said the authors.

Dr. Butt's team studied a national sample of 34,480 HCV infected subjects versus a non-infected control of the same number from the Electronically Retrieved Cohort of HCV Infected Veterans (ERCHIVES) and found that those infected were more likely to have a shortened survival rate. "HCV increased the risk of death by about 37% after adjusting for demographic characteristics and common comorbidities." Treatment for HCV was associated with a significant decrease in mortality. Individuals who received at least 48 weeks of

treatment had the lowest mortality, while those who received less than 48 weeks of treatment had intermediate mortality compared with untreated individuals. "Strategies to identify appropriate candidates for treatment, and to ensure completion of treatment may substantially reduce mortality in HCV infected persons," concluded the authors.

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