Research associates pro-inflammatory molecules with early death in HIV patients

January 16 2014

A study led by researchers at Boston University School of Medicine (BUSM) provides new insight into the impact that pro-inflammatory molecules have on early death in HIV patients who abuse alcohol. The findings, published online in the journal *AIDS*, pinpoint the inflammatory markers most associated with early death and may help explain why some patients die earlier than others even when all of these patients are on antiretroviral therapy.

Daniel Fuster, MD, PhD, a researcher at the Clinical Addiction Research and Education (CARE) unit at BUSM, is the study's lead author. Unique in its investigation of inflammatory markers in HIV and alcohol abuse, the study is the product of collaboration between Boston University School of Public Health, Boston Medical Center and the University of Pittsburgh Graduate School of Public Health.

Although breakthroughs have been accomplished in HIV antiretroviral therapy, some patients fare better than others. Factors influencing these differences have been identified, including co-infection with hepatitis viruses (especially hepatitis C), substance abuse (alcohol, as well as other drugs), noncompliance with antiviral drugs, CD4+ cell count and HIV viral load. Additionally, researchers have previously identified pro-inflammatory molecules called cytokines that have been associated with elevated HIV viral loads and more advanced HIV disease. Independently, alcohol abuse and chronic hepatitis C infection have also been associated with higher levels of inflammation in the bodies of HIV infected persons. However, it was previously unknown if the elevated

inflammatory state in these patients was due to their HIV or other independent risk factors.

Investigators recruited 400 HIV positive subjects who were known to abuse alcohol chronically. Half of these subjects also had chronic hepatitis C. They were followed for a three- to five-year period during which clinical information and laboratory samples were collected. Levels of seven well-known pro-inflammatory cytokine molecules were measured at baseline. From the beginning of the study in 2001 until data gathering was concluded in 2009, all patients were tracked in a national database to verify their survival status.

Based on this analysis, the researchers found that at the end of the study period, 85 out of the original 400 patients had died. Although these patients represent a population already at high risk of mortality from many problems (smoking, drug abuse, homelessness, etc.), most deaths in the study period were a result of either HIV or hepatitis C. Adjusting for known risk factors, such as age, smoking and hepatitis status, the researchers found that an increased burden of inflammation was strongly associated with increased mortality in alcohol-abusing HIV patients. This association was found, regardless of whether or not patients were taking their antiretroviral drugs. One inflammatory molecule in particular, known as interleukin-6 (IL-6) was found to have the strongest association with mortality among patients in the study.

"Current antiretroviral drug regimens may be able to improve mortality in most patients, but are unable to decrease the potentially dangerous burden of a chronic inflammatory state in the body," said Fuster. "Additional research should explore how to better manage chronic inflammation in these patients."

Provided by Boston University Medical Center