Older men more likely than women to die after pneumonia

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Differing biological response to infection between men and women may explain higher death rates among older men who are hospitalized with community-acquired pneumonia (CAP). The findings, published online in the *Critical Care Medicine* journal, may have important implications for understanding sex differences in life expectancy.

"Our study found that men with CAP were less likely to survive after an infection compared to women and this was not explained by differences in demographics, health behavior, chronic health conditions or quality of care," said Sachin Yende, M.D., assistant professor in the Department of Critical Care Medicine at the University of Pittsburgh School of Medicine and corresponding author of the study.

The researchers measured blood levels of inflammatory indicators, including tumor necrosis factor (TNF) and interleukins 6 and 10, coagulation indicators including Factor IX, and fibrinolysis indicators including D-dimer concentrations. They found patterns in these biomarkers that suggest men generate a stronger inflammatory and coagulation response and, perhaps, break up blood clots more quickly than women in response to infection. "These differences in inflammatory, coagulation and fibrinolysis biomarkers among men may explain the reduced short-term and long-term survival," said Dr. Yende.

Data were gathered from the multicenter Genetic and Inflammatory Markers of Sepsis (GenIMS) study. Participants were enrolled upon emergency department admission at 28 academic and community

hospitals in Pennsylvania, Connecticut, Michigan and Tennessee from 2001 to 2003. The study included 2,320 subjects, with a mean age of 64.9 years, 1,136 of whom were men. The men were sicker on admission, more likely to be smokers, and had at least one chronic health condition, such as cardiac disease or cancer. Severe sepsis occurred in 588 (31 percent) subjects. Of these, about half had severe sepsis on their first day of hospitalization.

Men had a higher risk than women of death at 30 days (7 percent vs. 4.5 percent), 90 days (11.4 percent vs. 8.6 percent) and one year (21 percent vs. 16 percent). "Even compared to women with an equivalent illness severity, men were more likely to die," Dr. Yende noted. "Survival differences persist up to one year after the initial hospitalization, when most patients had recovered from the pneumonia and left the hospital."

"To our knowledge, this is the largest study comparing biological response to infection between men and women. Our results suggest that immune response to infection may be an important target for interventions to reduce sex disparities in the outcomes of infections," said senior author Derek C. Angus, M.D., professor and chair in the Department of Critical Care Medicine at the University of Pittsburgh School of Medicine and principal investigator of the study.

"More studies will be needed to determine why the biological response differs between men and women," said Dr. Yende. "A clearer understanding may be useful toward designing interventions specifically targeted to men or women."

The GenIMS researchers hope to identify whether certain changes in the genes for key inflammatory molecules are associated with the risk of developing pneumonia, and the risk of progression to severe sepsis, septic shock, organ dysfunction or death. Because pneumonia is the most common cause of sepsis, patients with this infection represent an

excellent clinical model for studying sepsis in a relatively homogeneous population.

In a paper published online on April 3 in The FASEB Journal, GenIMS researchers led by Drs. Yende and Angus found that people with certain gene variations associated with higher levels of macrophage migration inhibitory factor, an innate immune response regulator, were less likely to die following CAP.

"Macrophage migration inhibitory factor is a molecule that plays an important role in inflammation and has been shown to worsen outcomes in animal models of sepsis. Our results are intriguing in light of these findings and as other research groups are trying to design human studies to block this molecule in sepsis," said Dr. Yende. In future work, the researchers will continue to examine relationships between sex and gene variations in CAP, sepsis and survival.

Source: University of Pittsburgh Schools of the Health Sciences (news : web)