U-shaped relationship of HDL and risk of infectious disease: two prospective population-based cohort studies.

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AIMS: Preclinical evidence has indicated that HDL may play an important role in the immune system; however, very little is known about the role of HDL in the immune system in humans. We tested the hypothesis that low and high concentrations of HDL cholesterol are associated with risk of infectious disease in the general population.

METHODS AND RESULTS: We included 97,166 individuals from the Copenhagen General Population Study and 9387 from the Copenhagen City Heart Study with measurements of HDL cholesterol at baseline. The primary endpoint was any infectious disease requiring hospital admission, ascertained in the Danish health registries from baseline in 2003-13 or 1991-94 through 2014; 9% and 31% of individuals in the two studies experienced one or more infectious disease events. Using restricted cubic splines, there was a U-shaped association between concentrations of HDL cholesterol and risk of any infection. Following multifactorial adjustment, individuals with HDL cholesterol below 0.8 mmol/L (31 mg/dL) and above 2.6 mmol/L (100 mg/dL) had hazard ratios for any infection of 1.75 (95% confidence interval 1.31-2.34) and 1.43 (1.16-1.76), compared to those with HDL cholesterol of 2.2-2.3 mmol/L (85-95 mg/dL). In the Copenhagen City Heart Study, corresponding hazard ratios for any infection were 2.00 (1.16-3.43) and 1.13 (0.80-1.60).

CONCLUSION: Low and high HDL cholesterol concentrations found in 21% and 8% of individuals were associated with higher risk of infectious disease in the general population. These findings do not necessarily indicate causality.

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