

# Low HDL cholesterol from gene variation not associated with increased risk of ischemic heart disease

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Lower levels of high-density lipoprotein (HDL) cholesterol due to a gene mutation is not associated with an increased risk of ischemic heart disease, according to a study in the June 4 issue of JAMA.

Numerous studies have indicated that a low plasma level of HDL cholesterol (the "good" cholesterol) is associated with an increased risk of ischemic heart disease (IHD), according to background information in the article. However, whether HDL cholesterol is a primary factor in the development of IHD is not clear, in part because of other factors related to low HDL cholesterol levels, such as plasma triglycerides, which may contribute independently to increases in cardiovascular events. "... studies of genetic disorders that lower HDL cholesterol without increases in plasma triglycerides and remnant lipoproteins provide an ideal system in which to assess the consequences of isolated, lifelong low HDL cholesterol levels," the authors write.

Ruth Frikke-Schmidt, M.D., Ph.D., of the University of Copenhagen, Denmark, and colleagues examined whether mutations in the gene ABCA1, which genetically reduce HDL cholesterol levels but do not increase plasma triglyceride levels, are associated with an increased risk of IHD. Three studies were used: the Copenhagen City Heart Study (CCHS), a 31-year general population study (n = 9,022; 28 heterozygotes [a person possessing two different forms of a particular gene, one inherited from each parent]); the Copenhagen General Population Study

(CGPS), (n = 31,241; 76 heterozygotes); and the Copenhagen Ischemic Heart Disease Study (CIHDS), (n = 16,623; 44 heterozygotes). Certain data in all three studies were collected during the period of January 1976 through July 2007, with researchers analyzing data on HDL cholesterol levels and the association between IHD and HDL cholesterol and genotype.

The researchers found that heterozygotes vs. noncarriers for 4 ABCA1 mutations (P1065S, G1216V, N1800H, R2144X) had HDL cholesterol levels of 41 mg/dL vs. 58 mg/dL, corresponding to a reduction in HDL cholesterol of 17 mg/dL. A 17 mg/dL lower HDL cholesterol level in the CCHS was associated with a 70 percent higher risk for IHD. However, for IHD in heterozygotes vs. noncarriers, the risk was 33 percent lower in the CCHS; 18 percent lower in the CGPS; and 14 percent lower in the CIHDS. When the studies were combined (n = 41,961; 6,666 cases; 109 heterozygotes), there was no association between heterozygotes and a higher risk of IHD.

"The principal finding of this study is that heterozygosity for loss-of-function mutations in ABCA1 associated with substantial, lifelong lowering of plasma levels of HDL cholesterol, but not with corresponding higher levels of plasma triglycerides or atherogenic [capable of producing a type of plaque in arteries] remnant lipoproteins, did not predict an increased risk of IHD," the authors write.

Source: JAMA and Archives Journals

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