

High C3 Molecule Levels May Indicate Type 2

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BY LAURA SUAREZ, ASSOCIATE EDITOR

Complement C3 is an inflammation-sensitive plasma protein (ISP) and a proinflammatory nonsecretory product that may be an indicator for elevated type 2 diabetes risk.¹

C3 is an interesting protein that is produced by the stimulation of proinflammatory cytokines, Dr. Duncan said. It has proinflammatory actions that alter that pathway of complement activation. The latter fact is not widely known.

As a proinflammatory marker generated by adipocytes, C3 has been found to have a strong inverse association to cross-sectional insulin sensitivity, said Bruce B. Duncan, MD, during a presentation at the American Diabetes Association 65th Annual Meeting and Scientific Sessions in San Diego.

"We know that adipocytes create several proteins, many of which have been shown to be involved in the pathogenesis of type 2 diabetes," he said.

TRANSPORTED IN ADIPOCYTES

ISPs act anabolically to indicated when energy is needed and also allows glucose to be transported in adipocytes and other cells, Dr. Duncan said. Previous studies have concluded that ISPs do indeed correlate with the development of diabetes.² Dr. Duncan and colleagues used the Atherosclerosis Risks In Community (ARIC) study to determine the involvement of a certain ISP – complement C3 – in the incidence of type 2 diabetes. This notion was tested across a large patient population from four areas in the United States.

Plasma samples were obtained and incidence of diabetes was checked in 1,100 black and white men and women selected from a cohort of 16,000 patients aged 45 to 64 years. This 7% sampling of the initial population was selected using ethnicity stratification to signify a community-based population. Baseline was in the late 1980s; over half (n=581) of the patients had diabetes by study design. Dr. Duncan defined diabetes with a fasting glucose \geq 126 mg/dL or a nonfasting glucose of 200 mg/dL.

These patients had elevated levels of complement C3 as determined by an immunoturbinate metric assay.

The relationship between C3 and diabetes episode was

evaluated using a proportional hazards ratio and adjusted for ethnicity, gender, smoking, body mass index and educational level. Blacks had a slight but statistically significant elevated level of C3 compared to whites (158 vs 145 mg/dL; 95% CI), Dr. Duncan. The same trend was seen in women compared to men.

The level of C3 in obese patients was higher than that in overweight and normal-weight patients.

The most interesting trend was that obese patients had heightened C3 levels when compared to those who were just overweight, he said, adding that C3 levels in overweight patients was higher than that in nonoverweight patients. The difference between C3 levels in obese and nonoverweight patients was 164 versus 136 mg/dL ($P<.001$).

Patients with the highest C3 levels had a fivefold greater risk of incident diabetes. After adjusting for triglycerides, adiponectin, leptin free fatty acids and fasting glucose, this became a twofold increase, Dr. Duncan concluded.

C3 production may occur by way of adipocytes or cells such as the liver's endothelial circulating inflammatory cells. When these levels are high, it may predict diabetes in middle-aged adults, Dr. Duncan said. "With respect to implications, these associations suggest that the previously described metabolic and inflammatory pathways of C3 may be of epidemiologic significance in the development of type 2 diabetes." ■

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1. Duncan BB. Complement C3 and the Development of Type 2 Diabetes Mellitus – The ARIC Study. Presented at the ADA 65th Annual Meetings and Scientific Sessions, June 10-14, 2005. San Diego.

2. Engstrom G, Hedblad B, Eriksson KF, et al. Complement C3 is a Risk Factor for the Development of Diabetes: A population-based cohort study. *Diabetes*. 2005;54:570-575.