

**Association Between Acute-Phase
Reactants and Advanced Glycation End
Products in Type 2 Diabetes**

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OBJECTIVE— Type 2 diabetes is associated with chronic low-grade inflammation, but the underlying mechanism(s) is not well understood. Because in vitro studies have shown that advanced glycation end products (AGEs) can trigger inflammatory responses, the present study has investigated whether serum concentration of AGEs is an important determinant of circulating levels of inflammatory markers, like C-reactive protein (CRP), in type 2 diabetic patients.

RESEARCH DESIGN AND METHODS— Diabetic patients ($n = 210$) and healthy control subjects ($n = 110$) of similar BMI were recruited. Serum AGEs were assayed by competitive enzyme-linked immunosorbent assay using a polyclonal rabbit anti-sera raised against AGE-RNase. Plasma high-sensitivity CRP was measured by an immunoturbidimetric assay and interleukin (IL)-6 by enzyme-linked immunosorbent assay.

RESULTS— Serum AGEs were increased in diabetic patients compared with control subjects (4.24 ± 0.88 vs. 3.15 ± 0.81 unit/ml, respectively, $P = 0.01$). Both plasma CRP ($1.55 [0.81-2.95]$ vs. 0.88 mg/dl [$0.51-1.89$], respectively, $P = 0.01$; median [interquartile range]) and IL-6 ($0.80 [0.68-0.97]$ vs. 0.69 pg/ml [$0.48-0.84$], respectively, $P = 0.01$) were also higher in diabetic patients than in control subjects. In the diabetic patients, log(CRP) correlated with AGEs ($r = 0.22$, $P = 0.002$) and with log(IL-6) ($r = 0.29$, $P = 0.001$). Forward stepwise linear regression analysis showed that BMI, log(IL-6), and AGEs were significant independent determinants of log(CRP) in the diabetic patients, accounting for 17, 12, and 10% of the variation in log(CRP), respectively.

CONCLUSIONS— Serum concentration of AGEs is increased in patients with diabetes and is an independent determinant of plasma CRP levels. Subclinical inflammation in these patients may therefore be partly due to activation of the inflammatory response by AGEs.

***Diabetes Care* 27:223–228, 2004**