

# Higher HDL May Protect Against Albuminuria in Type 1

The natural history of diabetic kidney disease in patients with type 1 diabetes is characterized by the onset of albuminuria.

BY MARK E. MOLITCH, MD

**H**igher levels of HDL cholesterol may be protective against the development of albuminuria in patients with type 1 diabetes.<sup>1</sup> Whether this is due to the HDL levels themselves or whether they serve as a marker for some other mechanisms requires further study.

Diabetes is the most common cause of kidney failure in the United States and among the most common causes worldwide.<sup>2</sup> Clinical trials and epidemiological studies have revealed that the most important risk factor for the development of diabetic kidney disease in type 1 patients is hyperglycemia.<sup>3,4</sup> Even so, we know that hyperglycemia cannot be the only determining factor as to who develops diabetic nephropathy. About one in three patients with type 1 diabetes will develop nephropathy, regardless of glycemic control. Therefore other genetic, metabolic and possibly environmental factors affect progression to diabetic nephropathy.

## CVD, NEPHROPATHY

There is a strong link between atherosclerotic cardiovascular disease and nephropathy, as demonstrated by many studies in both type 1 and 2 diabetes.<sup>5-8</sup> Hypertension and dyslipidemias are risk factors, and increased LDL levels have been found to be a risk factor in nephropathy in type 1 diabetes.<sup>9,10</sup> While elevated HDL is cardioprotective, as shown in many studies, this parameter has not been evaluated as a potential protective mechanism against nephropathy.<sup>11,12</sup>

My colleagues and I from the Northwestern University Feinberg School of Medicine in Chicago, analyzed the lipid profiles of patients who had type 1 diabetes for at least 20 years. Among them, 42 had albuminuria — 28 microalbuminuria and 14 macroalbuminuria — and 65

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did not have increased albumin excretion before intervention with statins or angiotensin-converting enzyme (ACE) inhibitors.

## SIMILAR STATISTICS

Among the two groups, age, sex, diabetes duration, total cholesterol, LDL and triglycerides were similar. By univariate analysis, we found significant differences ( $P<.01$ ) in HDL (albuminuria 1.42 mmol/L, no albuminuria 1.71 mmol/L,  $P<.01$ ), HbA1c (albuminuria 8.5%, no albuminuria 7.5%), and proportions with no, background and proliferative retinopathy (albuminuria 2.4%, 16.7% and 81%; no albuminuria 24.6%, 52.3% and 23.1%, respectively).

When we adjusted these results for age and sex, a 0.26-mmol/L increase in HDL is associated with an odds ratio (OR) of 0.70 (95% CI 0.54-0.90) for having albuminuria. In a multivariate model that adjusted for age, sex, diabetes duration and HbA1c, for every 0.54 mmol/L increase in HDL, patients are approximately half (OR 0.51 [95% CI 0.30-0.86]) as likely to have albuminuria, even after controlling for HbA1c.

Our patients with long-term disease and no microalbuminuria also had less severe retinopathy, only 23% of them having proliferative disease compared with 81% of those with albuminuria. This clustering of microvascular complications has been demonstrated by a number of previous stud-

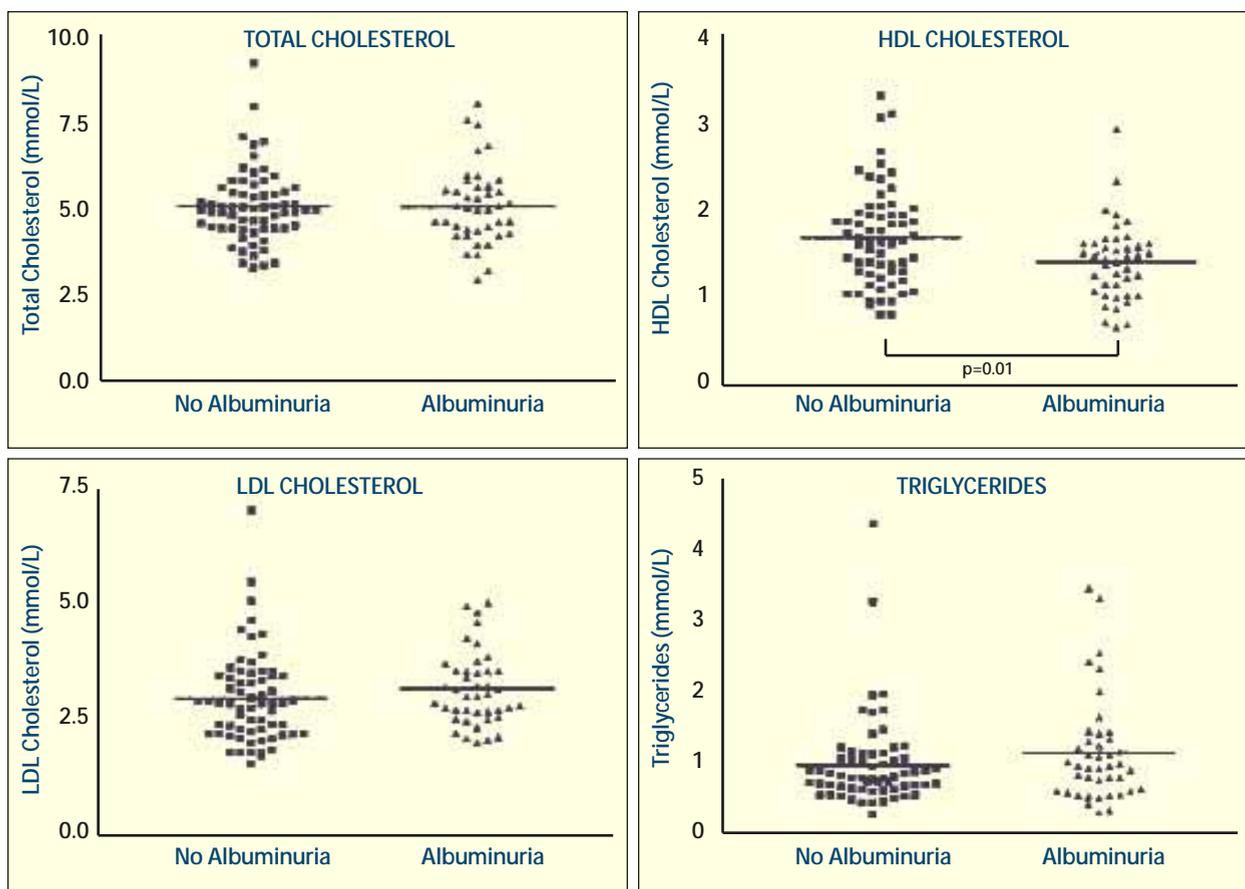


Figure 1. HDL cholesterol levels and albuminuria. The total cholesterol (top, left); HDL cholesterol (top, right); LDL cholesterol (bottom, left); and triglyceride levels (bottom, right) in patients with normal albumin excretion and those with albuminuria.

ies. Whether the protective effects of high HDL on coronary artery disease and nephropathy will correlated with each other can only be determined by long-term studies.

It is thought that HDL is not only involved in reverse cholesterol transport but also may have a number of other beneficial effects on the vascular endothelium. This effect on the vascular endothelium may explain the mechanism through which HDL has a salutary effect on the glomerulus. But, it may also be that the HDL level just serves as a marker for some other mechanisms. It should be emphasized that what we are reporting here is just an association; cause and effect remains to be clarified. Furthermore, there are no data suggesting that altering HDL levels through some intervention has any effect on the development of albuminuria. ■

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