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Lipoprotein(a), type 2 diabetes and nephropathy; the mystery continues

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Studies suggested that serum lipoprotein (a) [Lp (a)] concentration may take part in aggravation of diabetic nephropathy. In contrast, some investigators believe that, the association of Lp (a) with diabetic nephropathy is likely to be weak or nonexistent. It seems that serum Lp (a) can be considered as a promising predictive factor for the diagnosis of earlier diabetic nephropathy, However, prospective studies are needed to determine its role.

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Lipoprotein (a) [Lp (a)] is an important cardiovascular risk factor in the general population (1-6). However, data on the risks conferred by Lp(a) in patients with diabetes mellitus specially in diabetic nephropathy are scarce and controversial and it is not well known, whether, in diabetic state, Lipoprotein (a) affects nephropathy. While various studies have shown that Lp(a) can be associated with diabetic complications, its association with diabetic nephropathy is still unclear (7). While atherosclerosis is a major complication associated with diabetes mellitus(DM), various studies has been focused

on elucidating the possible role of Lp(a) in this disease, when epidemiological studies have implicated high levels of plasma lipoprotein(a) with increased risk for atherosclerotic cardiovascular disease(8). However, controversy exists as to whether lipoprotein(a) directly influences the nephropathy of diabetes(9). It was previously shown that, Lp(a) levels can be considered an independent risk factor for the development of atherosclerosis in type 2 diabetes(T2D) (10). It was assumed that, glycation of proteins, ie, nonenzymatic glycosylation resulting from the high plasma glucose levels found in diabetes,

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is thought to be one of the factors contributing to the severity of this disease. Indeed glycation produces modest increases in the degradation rate of Lp(a). However, glycation does not appear to enhance the atherogenic potential of unmodified Lp(a) significantly (8). In contrast, it was shown that Lp(a) was associated inversely with risk of type 2 diabetes independently of risk factors, in contrast to prior findings of positive associations of Lp(a) with cardiovascular risks (11). Similarly, the effect of Lp(a) on the risk factors of cardiovascular disease among diabetic patients might be different from that in the general population (11,12). Diabetes status may even attenuate the relation between Lp(a) and cardiovascular risk (12). Studied showed that high Lp(a) level and diabetes mellitus are independent markers of a greater extent of intracranial large-artery occlusive disease. These findings support the role of Lp(a) in intracranial stenotic atherogenesis and might be useful for the selection of high-risk patients (13). Also, available data showed that high Lp(a) level seems to be an independent risk factor for myocardial infarction in this T2DM cohort (14). It was also found that T2D had significant effects on Lp(a) concentrations (15,16). To evaluate the association of Lp(a) and hypertension (HTN) as a part of diabetic nephropathy aggravation, Nasri conducted a study on T2D patients (17), who were under treatments of oral hypoglycemic agents or insulin injections (17). He studied 122 patients, 82 females and 40 males with a mean age of 63 ± 10 years and duration of Diabetes mellitus and HTN of 7.4 ± 5.8 and 3.2 ± 4.6 years, respectively. The mean systolic and diastolic blood pressure (BP) were 138 ± 23 mmHg and 83 ± 12 mmHg, respectively. The mean serum Lp(a) was 22.2 ± 24.7 mg/dL (median: 18.3 mg/dL), and serum Lp(a) levels > 30 mg/dL was found in 29

(23.8%) patients. There were significant positive correlations duration of DM and duration of hypertension, with serum Lp(a). He suggested that kidney function is an independent determinant of Lp(a) and HTN in diabetic patients (17). In addition, they concluded that Lp(a) may have important implications for the increased susceptibility to vascular disease in diabetic patients (17). Whether Lp(a) is an independent risk factor for deteriorating renal function in type 2 diabetic patients with nephropathy? In a prospective study in type 2 diabetic patients with overt proteinuria, Song et al. demonstrated that Lp(a) is an independent risk factor for the progression of diabetic nephropathy in T2D with overt proteinuria, and is an independent predictor of the progression of diabetic nephropathy (18). The mechanism by which elevated Lp(a) levels might adversely affect the progression of diabetic nephropathy is not well known. It may be due to the atherogenic effect of Lp(a) which leads to renal ischemia because of increased atherosclerotic renal artery stenosis (18). In addition to vascular injury, Lp(a) might be implicated in glomerular injury (19). Lp(a) and oxidized Lp(a) have been shown to induce activation of reactive oxygen metabolites in isolated rat glomeruli (18,19). While Nakhjavani et al. (20) showed the significant difference of Lp(a) between males and females with a female preponderance, in another study conducted by Onuma et al., a possible role for Lp(a) as an independent risk factor for diabetic retinopathy in male patients with T2D was suggested (21). They showed that, in T2D patients, Lp(a) levels are elevated compared to non-diabetic subjects, and that higher Lp(a) levels are associated with higher prevalence of coronary artery disease and of retinopathy (22). Similarly, in a study on 76 insulin dependent diabetic patients, Kapelrud et al. found that serum

concentration of Lp(a) lipoprotein are twice as high in insulin dependent diabetic patients with microalbuminuria as in those without microalbuminuria. They concluded that increased concentrations of Lp(a) lipoprotein might partly explain the increased morbidity and mortality of cardiovascular disease observed among patients with diabetic nephropathy (22). Likewise, in a study conducted in China on a group of diabetic patients, the relationship between lipoprotein(a) level and progression of early diabetic nephropathy and also the significance of lowering of serum Lp(a) in preventing the progression of early diabetic nephropathy, was studied. Study was conducted on a group of non-diabetic controls and T2D including 90 patients without DN and 96 with microalbuminuria. Ninety-six patients with early diabetic nephropathy were randomly divided into control group and treatment group which was treated with 40 microgram of oral fluvastatin every night in addition to routine therapy. They found that, Lp(a) was significantly decreased in treatment group, accompanied by decrease in urinary albumin and serum creatinine. They concluded that, Increased serum Lp(a) may be associated with the progression of early diabetic nephropathy. Lowering serum Lp(a) can ameliorate microalbuminuria and improve renal function in patients with early diabetic nephropathy (23). Also, in a similar study in china, lowering serum Lp(a) by the same drug can ameliorate microalbuminuria and postpone the occurrence of renal failure in T2D (24). In conclusion, studies have suggested that serum Lp(a) concentration may take part in aggravation of diabetic nephropathy. In contrast, some investigators, believe that, the association of Lp(a) with diabetic nephropathy is likely weak or nonexistent. It seems that serum Lp(a) can be considered as a promising predictive factor for

the diagnosis of earlier nephropathy. However, more prospective studies are needed to determine such a role.

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