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Letter regarding normal albuminuria in patients with autopsy-proven advanced diabetic nephropathy

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Letter to The Editor

In the 2021 December issue of KI Rep Sasaki et al. point out that nearly half of 106 Japanese patients with a stage IIa- or higher diabetic-glomerulopathy, evident on autopsy, were "normoalbuminuric" (UACR < 30 mg/G) up to 3 years before death (1). While addressing this enigma, they ignored the mitigating impact of tubular handling of filtered albumin on albuminuria. About 3.2 grams of albumin and additional 10 grams of low-molecular proteins are normally filtered daily and are almost entirely uptaken or degraded along the nephron (2). Over 70% of filtered albumin is reabsorbed in proximal tubules in rats, and the rest is uptaken by distal nephron-segments. Proximal tubular reclaim of filtered albumin declines in early experimental diabetes in rats (3) while distal tubular reuptake is reciprocally enhanced (3). Tubular uptake of albumin leads to the formation of endocytic vesicles with lysosomal breakdown to amino acids that re-circulate into the bloodstream. Paracellular reclaim of albumin likely takes place as well (2), as is albumin degradation by brush-border enzymes with urinary clearance of albumin fragments and amino-acids.

Thus, diabetic nephropathy may be concealed if filtered albumin is fully reclaimed and degraded, while overt albuminuria reflects glomerular leak of albumin beyond the tubular reabsorptive capacity. Importantly, proteinuria per se induces tubuointerstitial damage and may reduce tubular capability of albumin reuptake (4). Therefore, we urge Sasaki and colleagues to further assess the presence and extent of non-glomerular parenchymal damage in their autopsy samples, anticipating a plausible inverse correlation of tubulointerstitial disease and albuminuria.
References


