Nephropathy

JOURNAL OF DIABETES AND ITS COMPLICATIONS

NA-CKD is more common in people with diabetes and with good control

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓

1 The study objective was to compare the prevalence and modifying factors of normoalbuminuric (NA) versus albuminuric (ALB) chronic kidney disease (CKD) in people with and without diabetes in the US.

2 The National Health and Nutrition Examination Survey (NHANES) is a programme of studies designed to assess the health and nutritional status of adults and children in the US; in this study data from NHANES 2001–2008 included 2798 people with diabetes and 15 743 without.

3 Age-specific prevalence of NA-CKD and ALB-CKD was calculated and stratified according to diabetes status, gender, ethnicity, mean arterial pressure >105 mmHg and HbA_{1c} >53 mmol/mol (7%); analyses were performed to determine odds ratios (ORs) and 95% confidence intervals (CIs) for NA-CKD.

4 The prevalence of NA-CKD rose with age, with an overall mean of 9.7% in participants with diabetes and 4.3% in those without diabetes; after adjustments, people with diabetes and near-normal HbA_{1c} had higher prevalence rates of NA-CKD than those with poor control.

5 NA-CKD was less prevalent in men with diabetes (OR, 0.58; 95% CI, 0.39–0.87) and in people who were black (OR, 0.44; 95% CI, 0.29–0.68) or from other ethnic groups (OR, 0.57; 95% CI, 0.34–0.96).

6 NA-CKD was more prevalent in people with diabetes, women and non-Hispanic white people within the setting of well-controlled glycaemia.

Mottl AK, Kwon K-S, Mauer M et al (2012) Normoalbuminuric diabetic kidney disease in the US population. *J Diabetes Complications* 24 Nov [Epub ahead of print]

Non-albuminuric chronic kidney disease in diabetes

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I decided against commenting on the important evidence paper summarised overleaf (Slinin et al 2012) in order to address the clinical problem of non-albuminuric chronic kidney disease (NA-CKD) in diabetes, which is something that we see a lot of in practice but is not so well understood.

In South Tees over 30% of people with diabetes have a reduced glomerular filtration rate (GFR) of <60 mL/min/1.73 m^2 (Nag et al, 2007), and the majority have a urine albumin:creatinine ratio of <3 mg/mmol. Over 50% of the UK Prospective Diabetes Study (UKPDS) cohort who developed an estimated creatinine clearance (eCC) <60 mL/min/1.73 m^2 never tested positive for albuminuria over 15 years of follow-up (Bilous, 2008).

The present study from the US (summarised alongside) found that 9.7% of the cohort of 2798 people, mostly with T2D, from the National Health and Nutrition Examination Survey (NHANES) 2001–2008 had NA-CKD, over double the rate seen in those without diabetes. The rates for albuminuric CKD (ALB-CKD) were 7.6% and 1.3% respectively for people with and without diabetes. Women and white, non-Hispanic individuals with diabetes were more likely to have NA-CKD, whereas an HbA_{1c} >53 mmol/mol (>7.0%) and mean arterial pressure >105 mmHg (approximately >155/80 mmHg) were associated with ALB-CKD.

Why is this important? The UKPDS showed that 16% of those with an eCC <60 mL/min/1.73 m^2 developed albuminuria later. Albuminuria is both an additive and multiplicative factor for cardiorenal morbidity and mortality in people with and without diabetes (Levey and Coresh, 2012). These data imply that it could potentially be preventable by better glycaemic and blood pressure control – perhaps not so startling information; however, as we know that rates of loss of GFR are significantly greater in those with albuminuria (Penno et al, 2011), then its prevention is a high priority. It also means that we can be more reassuring to our patients when they present with a GFR <60 mL/min/1.73 m^2 if they are negative for albuminuria, while at the same time emphasising the importance of achieving their glycaemic and blood pressure targets.

Sadly, only 53% of individuals with diabetes with ALB-CKD in the NHANES study were on renin–angiotensin system-blocking agents, which are the most potent albuminuria-lowering agents we have; thus there is much room for therapeutic improvement.

What might be the pathophysiological basis of NA-CKD in people with diabetes? Hyperglycaemia might play a role as the rates are higher in those with, as opposed to those without, diabetes. However, the increased prevalence of hypertension and macrovascular disease in people with diabetes may also be factors in their own right. There have been no unselected renal biopsy studies in those with NA-CKD compared with ALB-CKD, although it is known that the latter display a range of pathologies. Around two-thirds of people with microalbuminuria and T2D have predominantly ischaemic and tubulointerstitial changes, and pathognomonic diabetes lesions are seen in only one-third (Fioretto et al, 1996). Individuals with T2D with increased albuminuria have much more typical diabetic glomerulopathy (White et al, 2000). The female preponderance for NA-CKD may imply a role for urinary tract infection, which is more common in diabetes. The reduced rates in non-white populations remain a puzzle and may reflect less macrovascular disease or a different natural history of declining GFR with ageing in different ethnic groups.

Bilous R (2008) Microvascular disease: What does the UKPDS tell us about diabetic nephropathy? *Diabet Med* **25**: 25–9

Fioretto P, Mauer M, Brocco E et al (1996) Patterns of renal injury in NIDDM patients with microalbuminuria. *Diabetologia* **39**: 1569–76

Levey AS, Coresh J (2012) Chronic kidney disease. *Lancet* **379**: 165–80

Nag S, Bilous R, Kelly W et al (2007) All-cause and cardiovascular mortality in diabetic subjects increases significantly with reduced estimated glomerular filtration rate: 10-year data from the South Tees Diabetes Mortality study. *Diabet Med* **24**: 12–6

Penno G, Solini A, Bonora E et al (2011) Clinical significance of non-albuminuric renal impairment in type 2 diabetes. *J Hypertens* **29**: 1802–9

White KE, Bilous RW for the Collaborative Study Group (2000) Type 2 diabetic patients with nephropathy show similar structural functional relationships to type 1. *J Am Soc Nephrol* **11**: 1667–73

"Glomerular filtration rate decline was faster in those with persistent hyperfiltration; hyperfiltration may contribute to onset or progression of nephropathy."

AMERICAN JOURNAL OF KIDNEY DISEASE

Outcomes not improved by intensive treatment of diabetes and CKD

Readability	✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

1 Following on from the publication of clinical practice guidelines for treating people with diabetes and chronic kidney disease (CKD), the US National Kidney Foundation commissioned this systematic review to evaluate data on the management of this group.

2 The aim was to determine whether clinical outcomes in individuals with diabetes and CKD were improved by intensive glycaemic control, treatment of dyslipidaemia and the use of medications to prevent or slow the progression of elevated albuminuria in those with controlled blood pressure.

3 A systematic review of the literature identified randomised controlled trials on the management of hyperglycaemia, dyslipidaemia and albuminuria in individuals with diabetes and CKD; for all interventions, all-cause mortality was the primary outcome.

4 Five studies comprising 27 159 people examined the effect of intensive management of glycaemic control on clinical outcomes in T2D; intensive treatment did not reduce the incidence of all-cause mortality despite some positive effects.

5 Eleven studies comprising 7539 people assessed lipid management; statins did not reduce all-cause mortality or stroke in adults with diabetes and CKD.

6 Intensive glycaemic control and lipid interventions do not improve clinical outcomes in individuals with T2D; more intensive management of this group with CKD has inherent risks.

Slinin Y, Ishani A, Rector T et al (2012) Management of hyperglycaemia, dyslipidaemia and albuminuria in patients with diabetes and chronic kidney disease. *Am J Kidney Dis* **60**: 747–69

DIABETES CARE

Glomerular hyper-filtration may lead to renal disease

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 The authors sought to determine the relationship between hyperfiltration (glomerular filtration rate [GFR] ≥120 mL/min/1.73 m^2), GFR decline and nephropathy in 600 hypertensive people with type 2 diabetes and normo- or microalbuminuria from two randomised studies testing the renal effect of trandolapril and delapril.

2 GFR was measured at baseline and every 6 months, glucose disposal rate was assessed at baseline and 1 year in a subgroup and albuminuria was measured by three timed overnight urine collections.

3 In total, 4593 GFRs were measured over a median (range) follow-up of 4.0 (1.75–8.11) years; GFR declined by 3.37 (5.71–1.31) mL/min/1.73 m^2 per year – three- to five-fold faster than in the general population.

4 GFR decline was faster in those with persistent hyperfiltration; hyperfiltration may contribute to onset or progression of nephropathy.

Ruggenenti P, Porrini EL, Gaspari F et al (2012) Glomerular hyperfiltration and renal disease progression in type 2 diabetes. *Diabetes Care* **35**: 2061–8

BMC NEPHROLOGY

People confused by renal care referral have poor awareness of complications

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 As part of the diabetic renal disease care pathway study, the authors explored whether there were differences between UK South Asian and white people with T2D and renal disease in terms of referral rates, self-care, attitudes to and experiences of care.

2 In total, 23 South Asian and 25 white people with T2D and renal disease were referred to specialist nephrology care; their experiences of the diabetic renal care pathway and of diabetes were recorded.

3 Confusion with the referral process was experienced by both groups, who cited a lack of information given before or at referral; language barriers worsened the confusion in the South Asian group.

4 Individuals who were confused with the process had a low awareness of the renal complications of diabetes; this highlights the need for ongoing education.

Wilkinson E, Randhawa G, Feehally J et al (2012) A multi-centre qualitative study exploring the experiences of UK South Asian and white diabetic patients referred for renal care. *BMC Nephrology* **13**: 157

AMERICAN JOURNAL OF NEPHROLOGY

PVD increases mortality rate in people starting RRT

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 The study objective was to determine the effect of vascular comorbidities such as coronary heart disease (CHD), peripheral vascular disease (PVD) and cerebrovascular disease (CeVD) on mortality in people with T2D commencing renal replacement therapy (RRT); 877 people were followed up until death or a median of 1.93 years.

2 At the start of RRT, 41% had CHD, 27% PVD and 16% CeVD; individuals with PVD had a 1.9-fold increased risk of mortality compared with those without, those with CHD a 1.5-fold risk and those with CeVD a 1.4-fold risk.

3 The hazard ratio for death was highest in those with PVD and either CHD or CeVD; further studies are needed on the prevention of PVD.

Kervinen M, Lehto S, Grönhagen-Riska C, Finne P (2012) Effect of vascular comorbidities on survival of type 2 diabetes patients on renal replacement therapy. *Am J Nephrol* **36**: 509–15