

Nephropathy



Pregnancy and diabetic nephropathy

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The management of pregnant women with diabetes and chronic kidney disease (CKD) is challenging as there is an increased risk of diabetic, pregnancy and renal complications. Women with diabetic nephropathy (DN) often have other microvascular disease, such as retinopathy, which will need enhanced surveillance, and may also have hypoglycaemia unawareness, making tight blood glucose control potentially hazardous. Many will be on antihypertensive medications, some of which may be contra-indicated or not licensed for use in pregnancy.

These women are more prone to pre-eclampsia, and of having both small- and large-for-gestational-age foetuses, with an increased risk of congenital malformation; all of which may require early delivery (Bell et al, 2012).

In normal pregnancy, by the end of the first trimester, glomerular filtration rate (GFR) increases to 40–50% above pre-pregnancy levels by mechanisms not yet completely understood. Late in the third trimester, GFR usually declines but not back to pre-pregnancy levels (Baylis et al, 1994).

In women with CKD, stable or increased GFR in the first trimester is usually a positive prognostic sign, at least as far as renal function is concerned; a reduction in GFR is, however, an ominous sign and careful assessment of the risk of continuing the pregnancy needs to be undertaken with the woman and her partner. Due to volume expansion, GFR values based upon serum creatinine-based estimating equations are not valid, so a truer estimate may need to be calculated from timed urine collections. Ordinarily, these are only recommended in women with serum creatinine concentrations >120 µmol/L at booking (Katz et al, 1980). It is very important to assess albuminuria as early as possible in pregnancy as women with increased levels are more prone to pre-eclampsia. If nephropathy is confirmed, then regular monitoring throughout pregnancy using either urine albumin:creatinine or protein:creatinine ratios is necessary as a small number of women can develop

overt nephrotic syndrome with massive proteinuria, which will require early delivery.

Most UK clinics will look after only a small number of such women which makes the report of Damm et al (summarised alongside) from a large specialist service in Denmark extremely useful. What can we conclude from this study?

1) Unsurprisingly perhaps, the prevalence of nephropathy is similar in pregnant and non-pregnant women with diabetes and is similar for T1D and T2D. Reassuringly, this implies no problems with fertility.

2) However, the preparation for pregnancy and identification and treatment of DN are not as efficient for women with T2D. These women also appear to develop kidney complications after a much shorter known duration of diabetes than their T1D counterparts.

3) An early estimate of GFR using timed clearances may be helpful in women with significant CKD at the outset of pregnancy.

4) Regular estimates of albuminuria and proteinuria are required throughout pregnancy in women with DN.

5) Women with DN need prophylactic aspirin to reduce the risk of pre-eclampsia (which is current NICE Clinical Guidance [2010]).

6) Antihypertensive therapy should be continued during pregnancy and a target blood pressure of <135/<85 mmHg appears safe. Some women may need up to four different classes of agents.

7) Pregnancy in women with DN is high risk and should be managed by specialist multidisciplinary teams. Hopefully, the ongoing national diabetes in pregnancy audit will better inform us as to how to achieve a successful outcome for our patients with DN.

Baylis C (1994) *Renal Disease in Pregnancy*. RCOG Press, London. 3–20

Bell R et al (2012) *Diabetologia* **55**: 936–47

Katz AI et al (1980) *Kidney Int* **18**: 192–206

NICE (2010) NICE, London. Available at: <http://guidance.nice.org.uk/cg107> (accessed 24.12.2013)

Diabetes Care

Nephropathy in pregnant women with T1D and T2D

Readability ////

Applicability to practice ////

WOW! Factor ///

1 The authors of this study compared the prevalence of diabetic nephropathy and microalbuminuria in pregnant women with either T1D or T2D.

2 Set in Copenhagen, Denmark, 220 women with T2D and 445 women with T1D were included in the retrospective study over a 5-year period.

3 Hypertensive therapy was initiated in pregnant women that had blood pressure ≥135/85 mmHg or albumin-creatinine ratio ≥300 mg/g. This is because antihypertensive treatment is shown to reduce the prevalence of preterm delivery in women with T1D and diabetes nephropathy or microalbuminuria.

4 Women were asked to supply two urine samples at 22 weeks into their pregnancy to detect diabetic nephropathy or microalbuminuria.

5 In total, 41 women had diabetic nephropathy or microalbuminuria in early pregnancy. There was no statistically significant difference between the prevalence of diabetic nephropathy or microalbuminuria between women with T1D or T2D.

6 Blood pressure was stable during pregnancy in the T1D and T2D groups with no statistically significant differences between them.

7 Antihypertensive therapy was used more frequently in women with T1D, and it did not seem to have a negative effect on the pregnancy. This could be because women with T2D were mainly treated at primary care centres rather than specialised diabetes centres like those with T1D.

Damm JA, Asbjörnsdóttir B, Callesen NF et al (2013) Diabetic nephropathy and microalbuminuria in pregnant women with type 1 and type 2 diabetes. *Diabetes Care* **36**: 3489–94

Diabetes Care

Cooked meat increases serum creatinine and lowers eGFR

Readability ✓✓✓✓
 Applicability to practice ✓✓✓✓
 WOW! Factor ✓✓✓

- The aim of this study was to examine the effect of a cooked meat meal compared to a non-meat meal on serum creatinine levels at various postprandial intervals. Cooked meat is known to increase creatinine levels, which lowers estimated glomerular filtration rate (eGFR). The experimental prospective study included healthy volunteers and individuals with T1D or T2D and chronic kidney disease (CKD) stages 1 & 2, 3A, 3B and 4 ($n=80$, 16 per group).
- Participants had a mean age of 67 years and 82.5% were male. Each meal contained approximately 54 g of protein and were consumed on two separate days by all participants.
- Postprandial and fasting blood samples were taken at 1, 2, 4 and 12 hours (the fasting sample).
- Four hours postprandial, the cooked meat meal increased serum creatinine levels, which significantly lowered eGFR in all the CKD subgroup compared to after the non-meat meal.
- This had led to some participants being misdiagnosed with more severe CKD (i.e. CKD 3B instead of 3A).
- Twelve hours after ingestion, there was no significant difference in serum creatinine levels after the cooked meat and the non-meat meals.
- The article proposes that blood samples obtained after overnight fasting should be used to give a more accurate measure of kidney function.

Nair S, O'Brien SV, Hayden K et al (2013) Effect of a cooked meat meal on serum creatinine and estimated glomerular filtration rate in diabetes related kidney disease. *Diabetes Care* 23 Sep [Epub ahead of print]

Diabetes Care

Factors affecting microalbuminuria in young people with T1D

Readability ✓✓✓✓
 Applicability to practice ✓✓✓✓
 WOW! Factor ✓✓✓

- Using data from the large T1D Exchange Registry, the objective was to investigate the factors associated with microalbuminuria in young people aged <20 years.
- Of the 7549 participants (from 67 US-based clinics), 4.4% presented with microalbuminuria.
- The factors associated with a higher frequency of microalbuminuria in the population were longer diabetes duration, older age, female sex, higher diastolic blood pressure, higher mean HbA_{1c}, and lower BMI ($P\leq 0.05$ for each multivariate analysis).
- Since age, diabetes duration and sex are non-modifiable factors, this paper highlights the importance of routine screening for microalbuminuria to ensure timely diagnosis and treatment.

Daniels M, DuBose SN, Maahs DM et al (2013) Factors associated with microalbuminuria in 7,549 children and adolescents with type 1 diabetes in the T1D Exchange clinic registry. *Diabetes Care* 36: 2639–45

Diabetes Care

Beta-cell function linked to microalbuminuria

Readability ✓✓✓✓
 Applicability to practice ✓✓✓
 WOW! Factor ✓✓✓✓

- The authors investigated the relationship between insulin sensitivity and beta-cell function with the incidence of diabetes-related complications in 672 adults with T2D.

Diabetologia

Dialysis: Survival rate differences

Readability ✓✓✓✓
 Applicability to practice ✓✓✓✓
 WOW! Factor ✓✓✓

- The survival rates of individuals undergoing dialysis were investigated in three groups: those without diabetes, those with diabetes as the primary renal disease and those with diabetes as a co-morbid condition.
- Data were used from the European Renal Association–European Dialysis and Transplant Association (ERA–EDTA), and participants ($n=11\ 419$) were monitored until transplantation, death or the study end (5 years). During the follow-up, 7584 (49%) participants died.
- Mortality was higher in individuals with diabetes as the primary renal disease than in individuals with diabetes as a co-morbid condition, adjusted for age, sex, country and malignancy (hazard ratio 1.20, 95% confidence intervals 1.10–1.30).
- This finding is consistent across age categories, sex, and initial treatment modality. This suggests that the extent of organ damage caused by diabetes can affect the survival of individuals receiving dialysis treatment.

Schroijen MA, van de Luitgaarden MW, Noordzij M et al (2013) Survival in dialysis patients is different between patients with diabetes as primary renal disease and patients with diabetes as a co-morbid condition. *Diabetologia* 56: 1949–57

- The upper Matsuda ISI quartile was negatively correlated with coronary artery calcification (CAC), whereas the upper Insulinogenic Index quartile was associated with a reduced risk of microalbuminuria, but only when diabetes duration was not considered.
- The authors concluded that reduced beta-cell function is linked to increased risk of microalbuminuria, whilst impaired insulin sensitivity is associated with CAC occurrence.

Mulvey CK, McNeill AM, Girman CJ et al (2013) Differential associations of oral glucose tolerance test-derived measures of Insulin sensitivity and pancreatic beta-cell function with coronary artery calcification and microalbuminuria in type 2 diabetes. *Diabetes Care* 15 Aug [Epub ahead of print]

“Blood samples obtained after overnight fasting will give a more accurate measure of kidney function.”