DIABETIC NEPHROPATHY

University of Edinburgh
MSc. Internal Medicine
s2129747

- Diabetic nephropathy (DN) is an important cause of morbidity and mortality in both type 1 and type 2 diabetes. (1) Among the causes of ESRD in the world, DM is accounted for 30–50%.(2)
- The hallmark of established DN is persistent albuminuria, with co-existing retinopathy and no evidence of alternative kidney disease. In T1DM, this definition is highly specific. But, there is greater heterogeneity in T2DM in clinical presentation and in epidemiology. This includes greater variation in the timing between diagnosis of diabetes and development of DN. (2)
- It is rare for DN to manifest in people with T1DM in the first 10 years following diagnosis, but between 10 and 20 years the incidence of DN is approximately 3% per year. (2)
- T2DM accounts for 90% of diabetes globally. Up to 3% of those with T2DM present with already developed albuminuria at time of diagnosis.(2)

RISK FACTORS

Major risk factors(1) include-
1. Poor glycaemic control
2. Long duration of diabetes
3. Presence of other microvascular complications
4. Ethnicity (e.g. Asians, Pima Indians)
5. Pre-existing hypertension
6. Family history of diabetic nephropathy
7. Family history of hypertension

A number of clinical characteristics have been described that are associated with higher risk of progression of DKD including severity of albuminuria, rate of eGFR decline,
systolic blood pressure, haemoglobin A1c,
serum uric acid. (2)

PATHOPHYSIOLOGY

Figure1: Pathophysiology of Diabetic nephropathy(3)

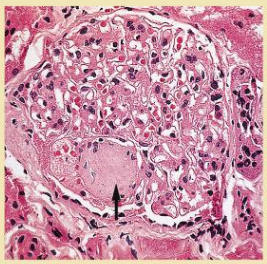

Figure 2: Nodular diabetic glomerulosclerosis.
There is thickening of basement membranes, mesangial expansion and a Kimmelstiel–Wilson nodule (arrow), which is pathognomonic of diabetic kidney disease. Source of the image:Elsevier.com. 2018. Davidson's Principles and Practice of Medicine - 23rd Edition. [online] Available at: <https://www.elsevier.com/books/davidsons-principles-and-practice-of-medicine/ralston/978-0-7020-7028-0> [Accessed 15 May 2022].

CLINICAL FEATURES

Diabetic nephropathy should be considered in patients who have diabetes mellitus (DM) and a history of one or more of the following:
• Passing of foamy urine
• Fatigue and foot edema
• Other associated disorders such as peripheral vascular occlusive disease, hypertension, or coronary artery disease.(3)

On physical examination,Patients may have physical findings associated with long-standing diabetes mellitus, such as the following:
• Hypertension
• Peripheral vascular occlusive disease (decreased peripheral pulses, carotid bruits)
• Evidence of diabetic neuropathy (decreased fine sensations and diminished tendon reflexes, nonhealing ulcers).(3)

INVESTIGATIONS

Screening: People with diabetes should have renal function and albuminuria measured at diagnosis and annually thereafter in T2DM; in T1DM, this can start from 5 years after diagnosis.(2)
Albuminuria is best assessed using ACR measurements on spot urine samples (ideally early morning samples).(2)
Renal function should be assessed using a serum-creatinine based eGFR calculation.(2)

Confirmation of persistent abnormalities: Clinical diagnosis of DN can be made when there is persistent moderate or severe albuminuria or a persistent reduction in eGFR to <60 mL/min/1.73 m2, occurring at least 5 years after onset of diabetes. In over 95% of cases, diabetic retinopathy is concurrently present.(2)

Renal Ultrasonography: In USG, kidney size is usually normal to increased in the initial stages and, later, decreased with chronicity.(3)

Renal Biopsy: Renal biopsy is not routinely indicated in all cases of DN. It is indicated if the diagnosis is in doubt, if other kidney disease is suggested, or if atypical features are present.(2,3) Classes I to IV are characterized by thickening of the glomerular basement membrane, mesangial expansion, nodular sclerosis (Kimmelstiel-Wilson lesion) and severe glomerulosclerosis, respectively.(2)

MANAGEMENT

01 Lifestyle Targets

- Physical activity>150 min/week aerobic activity.(2)
- >5% weight loss if BMI ⩾ 25 kg/m2.(2)
- Smoking cessation is recommended.(2)
- Dietary sodium should be <2300 mg/day.(2)

02 Glycaemic control

- HBA1C<7% for most patients.(2)
- SGLT2i is recommended who require another drug added to metformin to attain target HBA1C or cannot use or tolerate metformin.(2)
- DPP-4 inhibitors are anti-inflammatory and anti-oxidative.So,process of glomerulosclerosis is delayed.(4)
- GLP-1 receptor agonists reduce the expression of AGE receptors.(4)
- Newer drugs undergoing trials include protein kinase C (PKC) inhibitors,advanced glycation end-products (AGE) inhibitors.(4)

03 Blood pressure

- BP target should be <130/80 mmHg if 10 year CV risk ⩾15%.(2)
- Inhibition of the RAAS is a cornerstone in the management of DN;RAASi (ACEIs & ARBs) is first-line antihypertensive.(1-4)

04 Lipid lowering drugs

- High-intensity statin is recommended for all patients aged 50-70 years with multiple CV risk factors.(2)

References:

1.Elsevier.com. 2018. Davidson's Principles and Practice of Medicine - 23rd Edition. [online] Available at: <https://www.elsevier.com/books/davidsons-principles-and-practice-of-medicine/ralston/978-0-7020-7028-0> [Accessed 15 May 2022].
2.Selby NM, Taal MW. An updated overview of diabetic nephropathy: Diagnosis, prognosis, treatment goals and latest guidelines. Diabetes Obes Metab. 2020 Apr;22 Suppl 1:3-15. doi: 10.1111/dom.14007. PMID: 32267079.
3.Batuman et al. Diabetic Nephropathy Guidelines:Medscape[internet] Nov 02, 2021[cited May15,2022]. Available from https://emedicine.medscape.com/article/238946-guidelines
4.Wang J, Xiang H, Lu Y, Wu T, Ji G. New progress in drugs treatment of diabetic kidney disease. Biomed Pharmacother. 2021 Sep;141:111918. doi: 10.1016/j.biopha.2021.111918. Epub 2021 Jul 19. PMID: 34328095.