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Diabetic kidney disease

The kidneys sometimes become diseased in people who have diabetes. In some cases, this can result in kidney failure. Controlling your blood pressure and glucose level helps to minimise complications such as heart disease and stroke. Medication is also available.

Diabetic kidney disease is a complication that occurs in some people with diabetes. It can progress to kidney failure in some cases. Treatment aims to prevent or delay the progression of the disease. Also, it aims to reduce the risk of developing cardiovascular diseases such as heart attack and stroke which are much more common than average in people with this disease.

To find out more about the kidneys and urine, see the leaflet called What do kidneys do?

What is diabetic kidney disease?

Diabetic kidney disease (diabetic nephropathy) is a complication that occurs in some people with diabetes. In this condition the filters of the kidneys, the glomeruli, become damaged. Because of this the kidneys 'leak' abnormal amounts of protein from the blood into the urine. The main protein that leaks out from the damaged kidneys is called albumin.

In normal healthy kidneys only a tiny amount of albumin is found in the urine. A raised level of albumin in the urine is the typical first sign that the kidneys have become damaged by diabetes. Diabetic kidney disease is divided into two main categories, depending on how much albumin is lost through the kidneys:

- Microalbuminuria: in this condition, the amount of albumin that leaks into the urine is between 30 and 300 mg per day. It is sometimes called incipient nephropathy.

- Proteinuria: in this condition the amount of albumin that leaks into the urine is more than 300 mg per day. It is sometimes called macroalbuminuria or overt nephropathy.

How does diabetic kidney disease develop and progress?

A raised blood sugar (glucose) level that occurs in people with diabetes can cause a rise in the level of some chemicals within the kidney. These chemicals tend to make the glomeruli more 'leaky' which then allows albumin to leak into the urine.

In addition, the raised blood glucose level may cause some proteins in the glomeruli to link together. These 'cross-linked' proteins can trigger a localised scarring process. This scarring process in the glomeruli is called glomerulosclerosis. It usually takes several years for glomerulosclerosis to develop and it only happens in some people with diabetes.

As the condition becomes worse, scarred tissue (glomerulosclerosis) gradually replaces healthy kidney tissue. As a result, the kidneys become less and less able to do their job of filtering the blood. This gradual 'failing' of the kidneys may gradually progress to what is known as end-stage kidney failure.

- **Microalbuminuria** is usually the first sign that diabetic kidney disease has developed. Over months or years, microalbuminuria may go away (especially if treated - see below), persist at about the same level, or progress to proteinuria.
- **Proteinuria** is irreversible. If you develop proteinuria it usually marks the beginning of a gradual decline in kidney function towards end-stage kidney failure at some time in the future.

How common is diabetic kidney disease?

Although diabetic kidney disease is more common in people with type 1 diabetes, there are more people with type 2 diabetes and diabetic kidney disease. This is because type 2 diabetes is much more common than type 1 diabetes.

Diabetic kidney disease is actually the most common cause of kidney failure. Around one in five people needing dialysis have diabetic kidney disease.

Note: most people with diabetes do not need dialysis.

For people with type 1 diabetes

Microalbuminuria or proteinuria (defined above) is rarely present at the time when the diabetes is first diagnosed. By five years after the diagnosis of diabetes, about 1 in 7 people will have developed microalbuminuria.

After 30 years, about 4 in 10 people will have developed microalbuminuria. Some people with microalbuminuria progress to proteinuria and kidney failure.

For people with type 2 diabetes

At the time the diabetes is first diagnosed, about 1 in 8 people have microalbuminuria and 1 in 50 have proteinuria. This is not because diabetic kidney disease happens straightaway in some cases but because many people with type 2 diabetes do not have their diabetes diagnosed for quite some time after the disease had begun.

Of those people who do not have any kidney problem when their diabetes is diagnosed, microalbuminuria develops in about 1 in 7 people and proteinuria in 1 in 20 people, within five years.

Diabetic kidney disease is much more common in Asian and black people with diabetes than in white people.

What are the symptoms of diabetic kidney disease?

You are unlikely to have symptoms with early diabetic kidney disease - for example, if you just have microalbuminuria (defined above). Symptoms tend to develop when the kidney disease progresses. The symptoms at first tend to be vague and nonspecific, such as feeling tired, having less energy than usual and just not feeling well. With more severe kidney disease, symptoms that may develop include:

- Difficulty thinking clearly.

- A poor appetite.
- Weight loss.
- Dry, itchy skin.
- Muscle cramps.
- Fluid retention which causes swollen feet and ankles.
- Puffiness around the eyes.
- Needing to pass urine more often than usual.
- Being pale due to anaemia.
- Feeling sick (nausea).

As the kidney function declines, various other problems may develop - for example, anaemia and an imbalance of calcium, phosphate and other chemicals in the bloodstream. These can cause various symptoms, such as tiredness due to anaemia, and bone 'thinning' or fractures due to calcium and phosphate imbalance. End-stage kidney failure is eventually fatal unless treated.

How is diabetic kidney disease diagnosed and assessed?

Diabetic kidney disease is diagnosed when the level of albumin in the urine is raised and there is no other obvious cause for this. Urine tests are part of the routine checks that are offered to people with diabetes from time to time. Urine tests can detect albumin (protein) and measure how much is present in the urine.

The standard routine urine test is to compare the amount of albumin with the amount of creatinine in a urine sample. This is called the albumin:creatinine ratio (ACR). Creatinine is a breakdown product of muscle.

A blood test can show how well the kidneys are working. The blood test measures the level of creatinine, which is normally cleared from the blood by the kidneys. If your kidneys are not working properly, the level of creatinine in the blood goes up. An estimate of how well your kidneys are working can be made by taking into account the blood level of creatinine, your age and your sex. This estimate of kidney function is called the estimated glomerular filtration rate (eGFR).

What increases the risk of developing diabetic kidney disease?

All people with diabetes have a risk of developing diabetic kidney disease. However, a large research trial showed that there are certain factors that increase the risk of developing this condition. These are:

- A poor control of your blood sugar (glucose) levels. (The greater your HbA1c level, the greater your risk.)
- The length of time you have had diabetes.
- The more overweight you become.
- Having high blood pressure. The higher your blood pressure, the greater your risk.
- If you are male.

This means that having a good control of your blood glucose level, keeping your weight in check and treating high blood pressure will reduce your risk of developing diabetic kidney disease.

If you have early diabetic kidney disease (microalbuminuria), the risk that the disease will become worse is increased with:

- The poorer the control of blood sugar levels. The greater your HbA1c level, the greater your risk.
- Having high blood pressure. The higher your blood pressure, the greater your risk.
- Smoking.

What are the possible complications?

End-stage kidney failure

In people with proteinuria (described above), end-stage kidney failure develops in approximately 1 in 12 people after 10 years. If this occurs then you would need kidney dialysis or a kidney transplant.

Cardiovascular diseases

All people with diabetes have an increased risk of developing cardiovascular diseases, such as heart disease, stroke and peripheral arterial disease. If you have diabetes and diabetic kidney disease, your risk of developing cardiovascular diseases is increased further. The worse the kidney disease, the further increased the risk. This is why reducing any other cardiovascular risk factors is so important if you have diabetic kidney disease (see below).

High blood pressure

Kidney disease has a tendency to increase blood pressure. In addition, increased blood pressure has a tendency to make kidney disease worse. Treatment of high blood pressure is one of the main treatments of diabetic kidney disease.

What is the treatment for diabetic kidney disease?

Treatments that may be advised are discussed below. Treatments aim to:

- Prevent or delay the disease progressing to kidney failure. In particular, if you have early diabetic kidney disease (microalbuminuria) it does not always progress to the proteinuria phase of the disease.
- Reduce the risk of developing cardiovascular diseases such as heart disease and stroke.

An angiotensin-converting enzyme (ACE) inhibitor

There are several types and brands of this type of medication. ACE inhibitors work by reducing the amount of a chemical called angiotensin II that you make in your bloodstream. This chemical tends to narrow (constrict) blood vessels. Therefore, less of this chemical causes the blood vessels to relax and widen and so the pressure of blood within the blood vessels is reduced.

ACE inhibitors are medicines that are often used to treat high blood pressure. However, the way they work also seems to have a protective effect on the kidneys and heart. This means that they help to prevent or delay the progression of the kidney disease.

An angiotensin-II receptor antagonist (AIIRA)

There are several types and brands of this type of medication. The ones available in the UK are: azilsartan, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan and valsartan. AIIRAs work in a similar way to ACE inhibitors. One may be used instead of an ACE inhibitor if you have problems or side-effects with taking an ACE inhibitor. (For example, some people taking an ACE inhibitor develop a persistent cough.)

> **Dr Krishna Vakharia**, 23rd March 2023
> The National Institute for Health and Care Excellence (NICE) has recommended a different medication called finerenone. This medication works differently to ACE and AIIRA. They have advised it can be used in people under certain conditions - and usually when the above two have been tried.

Good control of your blood glucose level

Good control of your blood sugar (glucose) level will help to delay the progression of the kidney disease and to reduce your risk of developing associated cardiovascular diseases, such as heart disease and stroke. Ideally, the aim is to maintain your HbA1c to less than 48 mmol/mol but this may not always be possible to achieve and the target level of HbA1c should be agreed on an individual basis between you and your doctor.

Good control of your blood pressure

Strict blood pressure control is likely to reduce the risk of developing cardiovascular diseases and prevent or delay the progression of kidney disease. Most people should already be taking an ACE inhibitor or AIIRA (described above). These medicines lower blood pressure.

However, if your blood pressure remains at 130/80 mm Hg or more then one or more additional medicines may be advised to lower your blood pressure to below this level.

Review of your medication

Certain medicines can affect the kidneys as a side-effect which can make diabetic kidney disease worse. For example, you should not take anti-inflammatory medicines unless advised to by a doctor. You may also need to adjust the dose of certain medicines that you may take if your kidney disease becomes worse.

Other treatments to reduce risk factors

A medicine to lower your cholesterol level is commonly advised. This will help to lower the risk of developing some complications such as heart disease, peripheral arterial disease and stroke.

Where relevant, to tackle lifestyle risk factors, which include:

- Stop smoking if you smoke.
- Eat a healthy diet. However, those with established kidney damage may need to reduce the protein in their diet and limit sodium, potassium and phosphorus intake.
- Keep your weight and waist in check. Those with established disease may need to increase calories, if they develop problems maintaining a healthy weight.
- Take regular physical activity.
- Cut back if you drink a lot of alcohol.

What is the outlook?

- If you have microalbuminuria (described above), this may clear away, especially with treatment.

- If you have proteinuria (described above), over time the disease tends to become worse and progress to end-stage kidney failure. However, the length of time this takes can vary and it may take years. If your kidneys do begin to fail you should be referred to a kidney specialist.
- Once the kidney function goes below a certain level then you will need kidney dialysis or a kidney transplant.
- A main concern is the increased risk of developing cardiovascular diseases. Cardiovascular diseases, such as heart attack and stroke, are the main causes of death in people with diabetic kidney disease. The treatments outlined above will reduce the risk of these occurring.

Further reading

- Management of diabetes; Scottish Intercollegiate Guidelines Network - SIGN (March 2010 - updated November 2017)
- Diabetes UK
- Type 1 diabetes in adults: diagnosis and management; NICE Guidelines (August 2015 - last updated August 2022)
- Diabetes (type 1 and type 2) in children and young people: diagnosis and management; NICE Guidelines (Aug 2015 - updated May 2023)
- Diabetic foot problems: prevention and management; NICE Guidelines (August 2015 - last updated October 2019)
- Type 2 diabetes in adults: management; NICE Guidance (December 2015 - last updated June 2022)
- Stewart MW; Treatment of diabetic retinopathy: Recent advances and unresolved challenges. World J Diabetes. 2016 Aug 25;7(16):333-41. doi: 10.4239/wjd.v7.i16.333.
- Kopel J, Pena-Hernandez C, Nugent K; Evolving spectrum of diabetic nephropathy. World J Diabetes. 2019 May 15;10(5):269-279. doi: 10.4239/wjd.v10.i5.269.
- Finerenone for treating chronic kidney disease in type 2 diabetes; NICE Technology appraisal guidance, March 2023

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