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A Study of Diabetic Complications On Kidney

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ABSTRACT

Diabetic nephropathy is the leading cause of end-stage renal disease worldwide and an independent risk factor for all cause and cardiovascular mortalities in diabetic patients. New insights into the molecular mechanisms that underlie the development and progression of micro vascular complications of diabetes including nephropathy are emerging rapidly from experimental and clinical studies. Chronic hyperglycemia is a major initiator of diabetic micro vascular complications. Activation of diacylglycerol (DAG)-protein kinase C (PKC) pathway, enhanced polyol pathway, increased oxidative stress, and overproduction of advanced glycation end products have all been proposed as potential cellular mechanisms by which hyperglycemia induces diabetic vascular complications. The DAG-PKC pathway contributes to vascular function in many ways such as the regulation of endothelial permeability, vasoconstriction, extracellular matrix synthesis/turnover, cell growth, angiogenesis, cytokine activation, and leukocyte adhesion. We will briefly review the current knowledge base regarding the pathogenic role for the activation of DAG-PKC pathway in diabetic nephropathy and other microvascular complications of diabetes. The results from animal studies and key clinical studies investigating specific effects of the PKC isoforms on the renal and other vascular tissues to induce diabetic complications are also reviewed.

Key Words: *Diabetic, Kidney complications.*

INTRODUCTION

Diabetes mellitus, or simply diabetes, is a group of metabolic diseases in which a person has high blood sugar, either because the pancreas does not produce enough insulin, or because cells do not respond to the insulin that is produced. This high blood sugar produces the classical symptoms of polyuria frequent urination), polydipsia(increased thirst) and polyphagia (increased hunger).

Types of diabetes mellitus (DM).

Type 1 diabetes

Type 1 diabetes mellitus is characterized by loss of the insulin-producing beta cells of the islets of Langerhans in the pancreas, leading to insulin deficiency. This type can be further classified as immune-mediated or idiopathic.

Type 2 diabetes

Type 2 diabetes mellitus is characterized by insulin resistance, which may be combined with believed to involve the insulin receptor.

Gestational diabetes

Gestational diabetes mellitus (GDM) resembles type 2 diabetes in several respects, involving a combination of relatively inadequate insulin secretion and responsiveness.

SYMPTOMS

In diabetes, the body is unable to absorb glucose which leads to a host of problems. Here are some of the symptoms that could indicate diabetes:

- Increase in appetite, Frequent urination, Feeling too thirsty
- Loss of weight, Feeling fatigued all day long , Frequent infections,
- Poor wound healing, High irritability,Depression, Blurred vision

CAUSES

- Genes ,Autoimmune destruction of beta cells
- Lack of physical activity, obesity Ageing Certain drugs Pancreatic disease or injury

DIAGNOSIS

Diabetes is diagnosed using blood tests, and the three tests used for diagnosing diabetes are:

1. A1C test or glycohaemoglobin test
2. Fasting Plasma Glucose (FPG) test
3. Oral glucose tolerance test (OGTT)

TREATMENT

If your diabetes can't be controlled with diet, exercise and weight control, your doctor may recommend anti-diabetic medications or insulin. Most people who have type 2 diabetes start with an oral medicine. Here are some of them:

1. **Drugs that act on pancreas**

Sulfonylureas lower blood glucose levels by increasing the release of insulin from the pancreas. These drugs decrease blood sugar rapidly.

2. Drugs that decrease the amount of glucose released from the liver

Biguanides (Metformin) decrease glucose production by the liver, decrease the absorption of glucose in the intestines and improve the body's resistance to insulin.

3.D**rugs that increase the sensitivity (response) of cells to insulin**

Thiazolidinediones lower blood glucose by increasing the sensitivity of the muscle and fat cells to insulin.

4.Drugs that decrease the absorption of carbohydrates from the intestine

Alpha glucosidase is an enzyme in the small intestine which breaks down carbohydrates into glucose. Acarbose is the drug that inhibits this enzyme.

5.Drugs that slow emptying of the stomach

Exenatide is a substance like gut hormone (GLP-1) that cannot be easily broken down. It slows stomach emptying, slows the release of glucose from the liver and controls hunger.

6.Insulin Injections – Insulin is the backbone of treatment for patients with Type 1 diabetes. Insulin is also important in Type 2 diabetes when blood glucose levels cannot be controlled by diet, weight loss, exercise and oral medicines. Different types of insulin are:

1. Rapid-acting insulin – starts working in about 15 minutes and lasts for 3 to 5 hours. There are 3 types of rapid-acting insulin: Insulin lispro, Insulin asp art and Insulin glulisine

2. Short-acting insulin (regular insulin) – starts working in 30 to 60 minutes and lasts 5 to 8 hours.

3. Intermediate-acting insulin (insulin NPH) – starts working in 1 to 3 hours and lasts 12 to 16 hours.

4. Long-acting insulin (insulin glargine and insulin detemir) – starts working in about 1 hour and lasts 20 to 26 hours.

EXAMS AND TESTS

A urine analysis may show high blood sugar. However, a urine test alone does not diagnose diabetes.

Your health care provider may suspect that you have diabetes if your blood sugar level is higher than 200 mg/dL. To confirm the diagnosis, one or more of the following tests must be done.

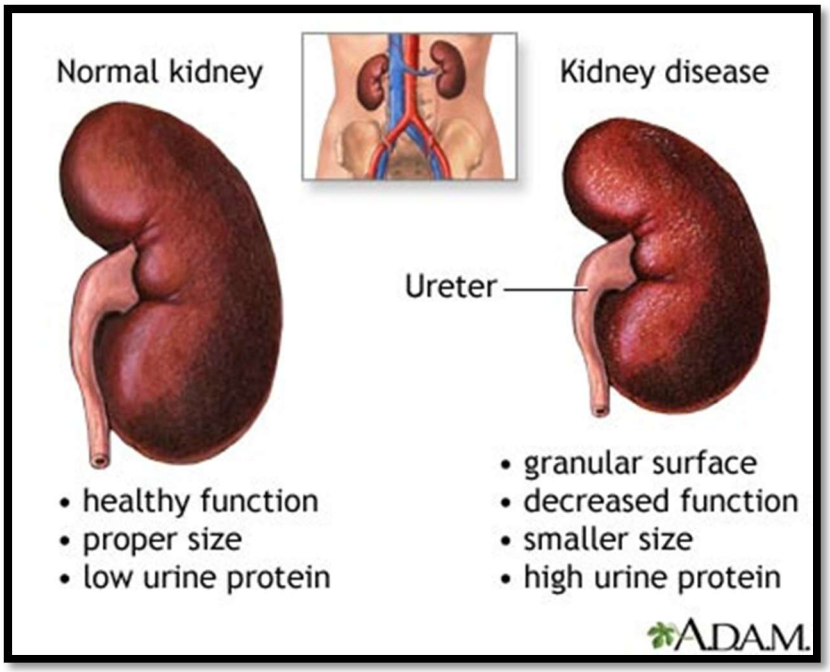
Blood tests:

- ✓ Fasting blood glucose level- diabetes is diagnosed if it is higher than 126 mg/dL twice. Levels between 100 and 126 mg/dL are called impaired fasting glucose or pre-diabetes. These levels are risk factors for type 2 diabetes.
- ✓ Hemoglobin A1c test
  - Normal: Less than 5.7%
  - Pre-diabetes: 5.7% - 6.4%
  - Diabetes: 6.5% or higher
- ✓ Oral glucose tolerance test - diabetes is diagnosed if glucose level is higher than 200 mg/dL after 2 hours of drinking a glucose drink. (This test is used more often for type 2 diabetes.)
- ✓ Screening for type 2 diabetes in people who have no symptoms is recommended for:

- ✓ Overweight children who have other risk factors for diabetes, starting at age 10 and repeated every 2 years
- ✓ Overweight adults (BMI greater than 25) who have other risk factors
- ✓ Adults over age 45, repeated every 3 years.

KIDNEY DISEASES

The kidneys filter and clean blood. Not surprisingly, having too much glucose in the blood puts a strain on them. Over time, this can actually lead to kidney failure. When this happens, dialysis or a kidney transplant may be needed.



DIABETES AND KIDNEY DISEASES Both types of diabetes can lead to kidney disease, but type 1 diabetes is more likely to lead to kidney failure. Diabetes is the most common cause of kidney failure, accounting for more than 40 percent of new cases.

Diabetes and Kidney Disease: An Overview

Each year in the United States, nearly 100,000 people are diagnosed with kidney failure, a serious condition in which the kidneys fail to rid the body of wastes. Kidney failure is the final stage of a slow deterioration of the kidneys, a process known as nephropathy.

PATHOPHYSIOLOGY OF KIDNEY

The kidneys act as filters to clean the blood. They get rid of waste and extra fluid. The tiny filters throughout the kidneys are called glomeruli.

Kidney Disease and Diabetes: The Course of Kidney Disease

Diabetic kidney disease takes many years to develop. In some people, the filtering function of the kidneys is actually higher than normal in the first few years of their diabetes. This process has been called hyperfiltration.Over several years, people who are developing kidney disease will have small amounts of the blood protein albumin begin to leak into their urine. At its first stage, this condition has been called microalbuminuria. The kidney's filtration function usually remains normal during this period.

Intensive Management of Blood Glucose

Intensive management is a treatment regimen that aims to keep blood glucose levels close to normal. The regimen includes:

- ✓ Testing blood glucose frequently
- ✓ Administering insulin frequently throughout the day on the basis of food intake and exercise
- ✓ Following a diet and exercise plan
- ✓ Consulting a healthcare team frequently.

Dialysis and Transplantation

When people with diabetes experience kidney failure, they must undergo either dialysis or a kidney transplant. As recently as the 1970s, medical experts commonly excluded people with diabetes from dialysis and transplantation, in part because the experts felt damage caused by diabetes would offset benefits of the treatments. Today, because of better control of diabetes and improved rates of survival following treatment, doctors do not hesitate to offer dialysis and kidney transplantation to people with diabetes.

STATISTIC ON KIDNEY DISEASES AND DIABETES

Diabetes is the most common cause of kidney failure, accounting for more than 40 percent of new cases. Even when drugs and diet are able to control diabetes, the disease can lead to nephropathy and kidney failure.

People with kidney failure undergo either:

- ✓ Dialysis, which substitutes for some of the filtering functions of the kidneys
- ✓ Transplantation to receive a healthy donor kidney.

DIABETIC NEPHROPATHY (KIDNEY DISEASE)

Diabetic Nephropathy

Nephropathy is the deterioration of kidney function. The final stage of nephropathy is called kidney failure, end-stage renal disease, or ESRD.According to the CDC, diabetes is the most common cause of ESRD. In 2011, about 26 million people in the U.S. were reported to have diabetes, and more than 200,000 people with ESRD due to diabetes were either on chronic renal dialysis or had a kidney transplant. Both type 1 and type 2 diabetes can lead to diabetic nephropathy, although type 1 is more likely to lead to ESRD.

Cause

Hypertension, or high blood pressure, is a complication of diabetes that is believed to contribute most directly to diabetic nephropathy. Hypertension is believed to be both a cause of diabetic nephropathy, as well as a result of the damage that is created by the disease. As kidney disease progresses, physical changes in the kidneys often lead to increased blood pressure.

Prevention

The onset and progression of diabetic nephropathy can be slowed by intensive management of diabetes and its symptoms, including taking medications to lower blood pressure.

Detection

You should have your urine tested at regular intervals to check for a protein called albumin. Normally, urine should not have any albumin. Having even a small amount of albumin in your urine is a sign that early kidney damage is present.

TREATMENT

Treatment may include any, or a combination of, the following:

- ✓ Proper diet
- ✓ Exercise
- ✓ Strict monitoring and controlling of blood glucose levels, often with medication and insulin injections
- ✓ Medication to lower blood pressure.

DIABETIC NEPHROPATHY DIAGNOSIS

- ✓ Urine tests are recommended once per year in people with type 1 diabetes, beginning about five years after diagnosis, and in people with type 2 diabetes, starting at the time of diagnosis.
- ✓ The urine test is looking for a protein called albumin. If there is albumin (protein) in your urine, it means you have diabetic nephropathy.
- ✓ The same urine test that is used to diagnose diabetic nephropathy will also be used to monitor your condition over time.

DIABETIC NEPHROPATHY COMPLICATIONS

- ✓ The key complication of diabetic nephropathy is more advanced kidney disease, called chronic kidney disease. Chronic kidney disease can, in turn, progress even

further, eventually leading to total kidney failure and the need for dialysis or kidney transplantation.

DIABETIC NEPHROPATHY TREATMENT

- ✓ Make healthy lifestyle choices
- ✓ Keep your blood sugar as close to normal as possible
- ✓ Keep your blood pressure below 130/80, if possible
- ✓ Limit the amount of salt you eat
- ✓ Lose weight if you are overweight
- ✓ Manage blood sugar levels —
- ✓ A blood test called A1C is also used to monitor blood sugar levels;

DIABETES AND ALL CAUSE MORTALITY

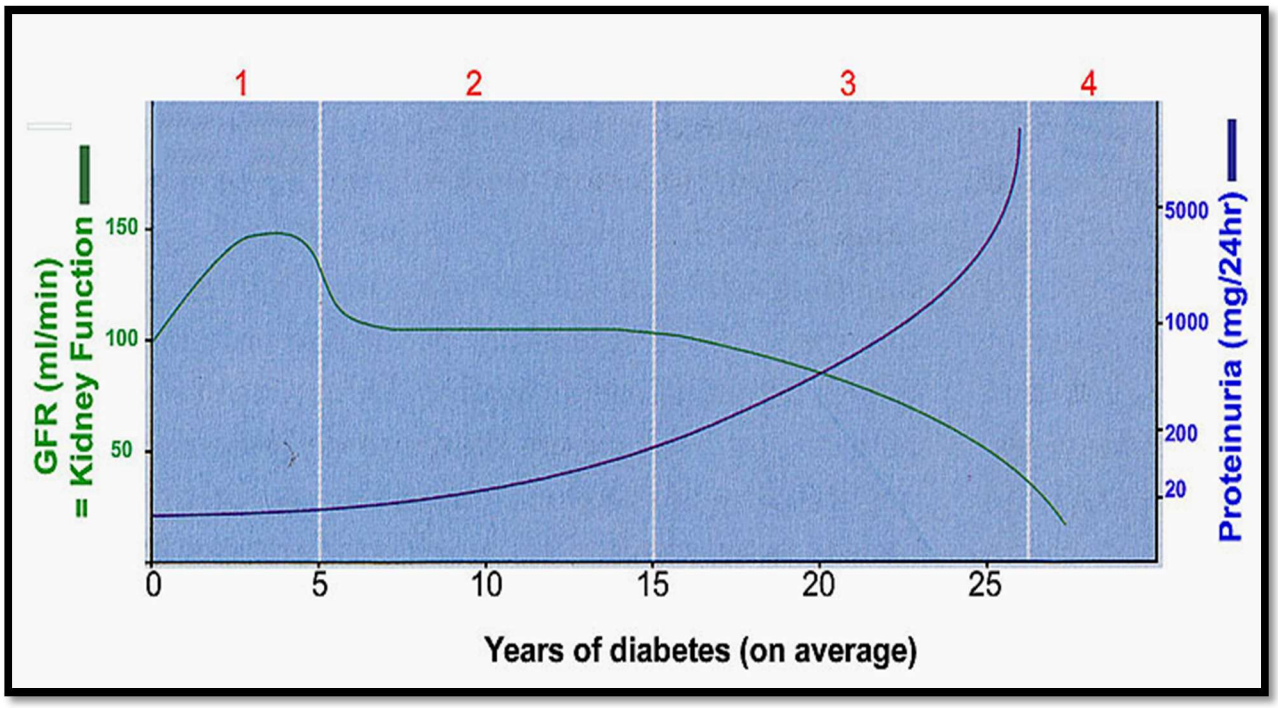
Mortality

Fewer than 5% of deaths among people with Type 2 diabetes are directly attributed to renal disease.

The majority of deaths result from myocardial infarction, heart failure or stroke.However, a eta-analysis of eight studies found that the death-rate among people with microalbuminuria was ore than double the rate in people with normal urinary albumin levels; risk ratios were 2.4 (95% CI, 1.8 to 3.1) and 2.0 (95% CI, 1.4 to 2.7) foroverall and cardiovascular mortality, respectively.

A 12-year study of 4,714 people with diabetes (both types) reported that proteinuria was associated with an eight-fold increase in deaths among women and a five-fold increase in risk among men, compared with those who did not have proteinuria.

Biochemistry and molecular cell biology of diabetic complications



There are 5 stages of Diabetic Nephropathy (Diabetic Kidney Disease):

Stage I: High Glomerular Filtration Stage.

The main features are the increase of Glomerular Filtration Rate (GFR) and the increase of size of the kidney.

Stage II: Normal Albuminuria Stage.
In this stage, urine albumin expelling(UAE) is normal (<20ug/min or < 30mg/24h). After exercise, the UAE will increase and it can recover after rest.
Stage III: Early Stage Diabetic Nephropathy (Diabetic Kidney Disease).
The main manifestations are UAE is continuously higher than 20～200μg/min (30～300mg/24h). High filtration is probably one cause of continuous micro albunminuria.
Stage IV: Clinical Diabetic Nephropathy Stage.
The features of this stage are large amount of albuminuria, UAE> 200μg/min, or continuous urine protein > 0.5g/d.
Stage V: Renal Failure Stage.
Once the continuous loss of urine protein develops to clinical Diabetic Nephropathy, the GBM will thicken widely, glomerular capillary lumens will become progressively narrow and there are necrotic glomeruli.

CONCLUSION

Diabetes is a slow killer with no known curable treatments. However, its complications can be reduced through proper awareness and timely treatment. Three major complications are related to blindness, kidney damage and heart attack. It is important to keep the blood glucose levels of patients under strict control for avoiding the complications. One of the difficulties with tight control of glucose levels in the blood is that such attempts may lead to hypoglycemia that creates much severe complications than an increased level of blood glucose. The goal of this project is to give a general idea of the current status of diabetic kidney complications.

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