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Diabetes and Their Complications

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ABSTRACT: Diabetes mellites (DM) is a chronic class of metabolic disorder which the main symptom associated with disease is high sugar level for long period. The hormone insulin moves the blood into your cells to be stored or used for energy. With diabetes, your body eighter doesn't make enough insulin or can't effectively use the insulin. There is mainly diabetes are classified into two groups, Type 1 & Type 2. In which one is insulin dependent & another one non-insulin dependent. untreated high blood sugar from diabetes can damage your nerves, eyes, kidneys, other vital organ of the body. The complications of diabetes may include possibly blindness, amputation of lower limb, renal failure, & cardiac arrest or stroke. This review summarizes pathophysiology of diabetes and at glance complications of the diabetes. This work is aimed to collect some the diabetes related complications are in one frame. It also elaborates the secondary messengers which plays the mechanism at the cellular level.

KEYWORDS: Diabetes mellites, peripheral artery disease, vascular damage, retinopathy, hormones.

I. INTRODUCTION

Diabetes is the metabolic disorder caused by the improper use of the hormone insulin. From the ancient times the diabetes mellites is continued with the people, DM is a serious, chronic and complex illness characterized by hyperglycaemia thatresulted from the pancreaticβ-cells generate deficient insulin (a hormone that adjusts blood glucose) when the body cannot efficiently custom the insulin or both of them. World health organization has categorized DM as the 7th leading cause in USA while it was estimated that 422 million adults present diabetes in 2014, 4 times higher than the recorded cases in 1980.

There is main two types of diabetes

i. Type - 1 insulin dependent.
ii. Type-2 non-insulin dependant

II. PATHPYSIOLOGY

Pathophysiology of type 1 diabetes

In this condition the immune system attacks and destroys the insulin producing beta cells of the pancreas. There is beta cell deficiency leading to complete insulin deficiency. Thus, is it termed an autoimmune disease where there are anti insulin or anti-islet cell antibodies present in blood. These cause lymphocytic infiltration and destruction of the pancreas islets. The destruction may take time but the onset of the disease is rapid and may occur over a few days to weeks. There may be other autoimmune conditions associated with type 1 diabetes including vertigo and hypothyroidism. Type 1 diabetes always requires insulin therapy, and will not respond to insulin-stimulating oral drugs.

Pathophysiology of type 2 diabetes

This condition is caused by a relative deficiency of insulin and not an absolute deficiency. This means that the body is unable to produce adequate insulin to meet the needs. There is Beta cell deficiency coupled with peripheral insulin resistance. Peripheral insulin resistance means that although blood levels of insulin are high there is no hypoglycaemia or low blood sugar. This may be due to changes in the insulin receptors that bring about the actions of the insulin. Obesity is the main cause of insulin resistance. In most cases over time the patients need to take insulin when oral drugs fail to stimulate adequate insulin release.

III. SECONADRY MESSENGER INVOLVE IN THE INSULIN SIGNALING

As this review paper inform us that, specific binding site for insulin are present on the plasma membranes of target tissues. In order to explain how insulin regulates a wide variety of biologic function both on the surface of the cell as well as in its interior, it has been postulated that

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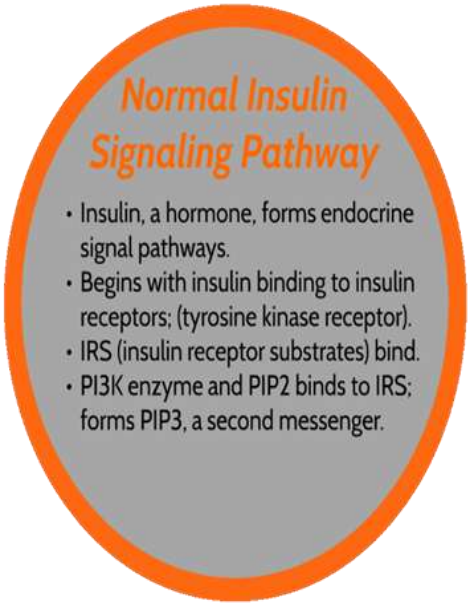
insulin generate a second messenger at the cell surface.

Up todate, however, no second messenger for insulin has been identified that can carry out all of insulin known action. Recent studies have demonstrated that, in addition to the plasma membrane, other subcellular organelles, such as the nucleus, have specific binding sites for insulin.

These most likely involve a complex network of pathways resulting in the coordination of mechanistically distinct cellular effects. Because the well-recognized mechanisms of signal transduction (i.e., cyclic nucleotides, ion channels) appear not to be central to insulin action, investigators have searched for a novel second-messenger system.

A low-molecular-weight substance has been identified that mimics certain actions of insulin on metabolic enzymes. This substance has an inositol glycan structure, and is produced by the insulin-sensitive hydrolysis of a glycosylphosphatidylinositol in the plasma membrane. This hydrolysis reaction, which is catalysed by a specific phospholipase C, also results in the production of a structurally distinct diacylglycerol that may selectively regulate one or more of the protein kinases C. The glycosyl-phosphatidylinositol precursor for the inositol glycan enzyme modulator is structurally analogous to the recently described glycosyl-phosphatidylinositol membrane protein anchor. Preliminary studies suggest that a subset of proteins anchored in this fashion may be released from cells by a similar insulin-sensitive phospholipase-catalysed reaction. Future efforts will focus on the precise role of the metabolism of glycosyl phosphatidylinositol in insulin action.



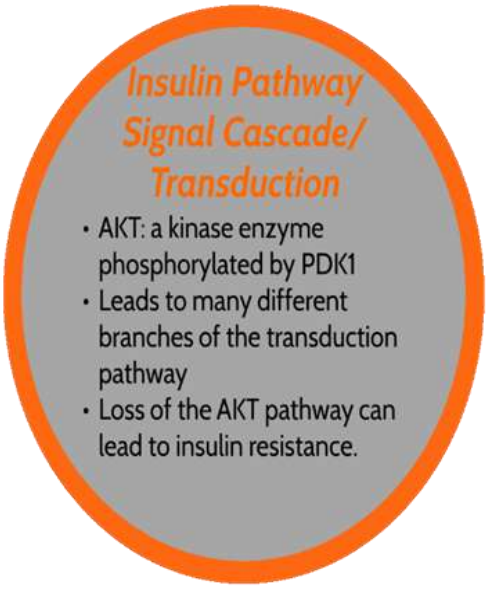


Fig 1.normal insulin sinaling pathwayFig 2. Insulin pathway signal cascade

This is all about the secondary messenger involved in the insulin signalling.

IV. COMPLICATIONS OF DIABETES

There is growing evidence that the underlying mechanisms in the pathogenesis of diabetic complications include oxidative stress created by the overproduction of reactive oxygen species (ROS) and defects in the insulin signal transduction pathway.

Diabetes is associated with the number of complications. Acute metabolic complications are associated with the mortality include diabetic ketoacidosis from exceptionally high blood concentration (hyperglycaemia) & coma as result of low blood glucose. There are lots of complication arises due to the diabetes, but this review will focus arguably the most devastating consequences of diabetes, its long-term complications i.e. retinopathy, nephropathy, heart diseases & vascular complications.

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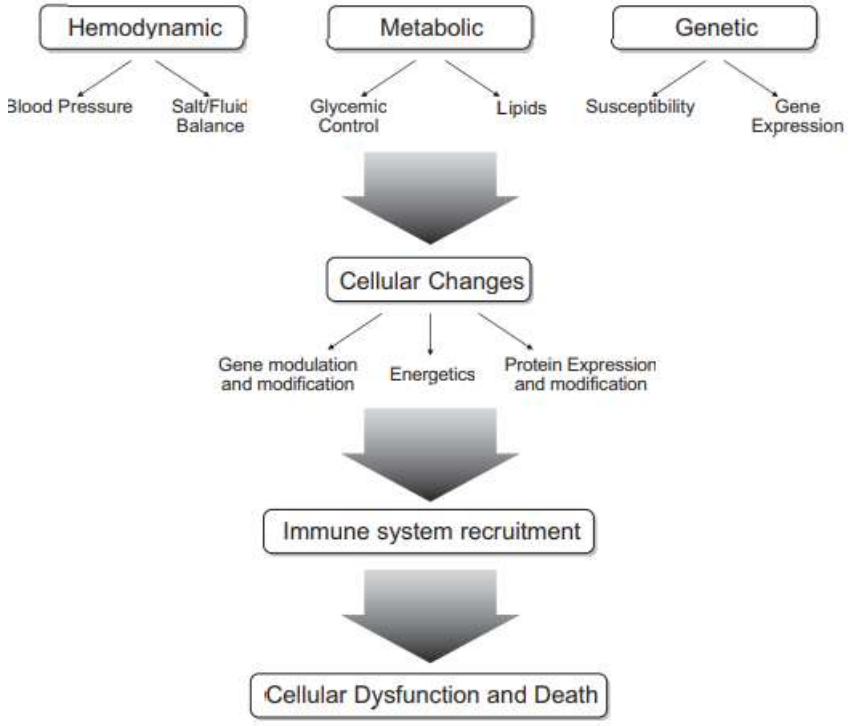

Fig. Represent the overview of the major areas contributing to diabetic complication.

1. RETINOPTHY

The diabetes is the most leading metabolic disorder. diabetes is not the single it came with the long-term clusters of the diseases and disorders.

Diabetic retinopathy is characterized by a spectrum of lesions within the retina and is the leading cause of blindnessamong adults aged 20–74 years. These includechanges in vascular permeability, capillary microaneurysms, capillary degeneration, and excessive formation ofnew blood vessels(neovascularization). The neural retina isalso dysfunctional with death of some cells,which altersretinal electrophysiology and results in an inability to discriminate between colours. Clinically, diabetic retinopathy isseparated intonon-proliferative and proliferative disease. In the early stages, hyperglycaemia can lead to intramural pericyte death and thickening of the basement membrane, which contribute to changes in the integrity of bloodvessels within the retina, altering the blood-retinal barrierand vascular permeability. In this initial stage of non-proliferative diabetic retinopathy (NPDR), most people donot notice any visual impairment.At first, diabetic retinopathy may cause no symptoms or only mild vision problems. Eventually, it can cause blindness.

The condition can develop in anyone who has type 1 or type 2 diabetes.If you have diabetes, it's important for you to get a comprehensive dilated eye exam at least once a year. Diabetic retinopathy may not have any symptoms at first — but finding it early can help you take steps to protect your vision. Diabetic retinopathy, also known as diabetic eye disease (DED),[2] is a medical condition in which damage occurs to the retina due to diabetes mellitus. It is a leading cause of blindness in developed countries.

Degeneration or occlusion of retinal capillaries are stronglyassociated with worsening prognosis (60), which is mostlikely the result of ischemia followedby subsequent releaseof angiogenic factors including those related to hypoxia.This progresses the disease into the proliferative phasewhere neovascularization and accumulation of fluid withinthe retina, termed macula edema, contribute to visual impairment. In more severe cases, there can be bleeding withassociated distorting of the retinal architecture includingdevelopment of a fibrovascular membrane which can subsequently lead to retinal detachment.

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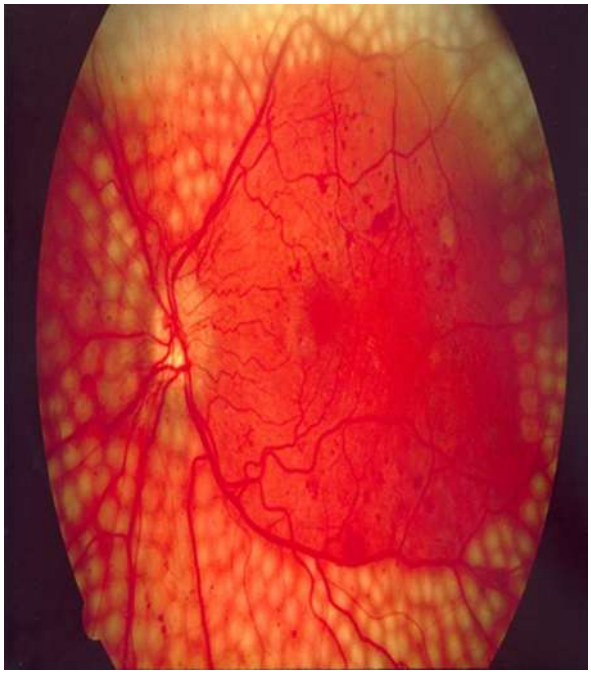

Fig. retina shows the edema.

In addition to maintenance of blood pressure and glycaemiccontrol, there are a number of treatments for diabetic retinopathy that have efficacy in reducing vision loss. Thesethree treatments include laser photocoagulation, injectionof the steroid triamcinolone, and more recently vascularendothelial growth factor (VEGF) antagonists into the eye,and vitrectomy, to remove the vitreous. However, there isno agreed medical approach to slow disease progressionbefore the use of these rather invasive treatments.

Diabetic retinopathy affects up to 80 percent of those who have had diabetes for 20 years or more. At least 90% of new cases could be reduced with proper treatment and monitoring of the eyes. The longer a person has diabetes, the higher his or her chances of developing diabetic retinopathy. Each year in the United States, diabetic retinopathy accounts for 12% of all new cases of blindness. It is also the leading cause of blindness in people aged 20 to 64.

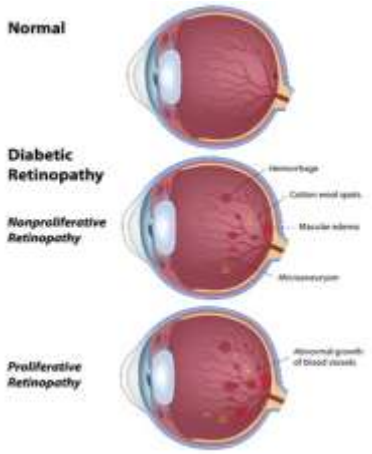

Fig. represent the phases of retinopathy.

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RECENT DETECTION TECHNIQUE OF DIABETIC RETINOPATHY.

In this there are three types of retinal observation
(1) screening of diabetic retinopathy
(2) retinal imaging
(3) diabetic retinopathy by CAD

The retinopathy by CAD subdivided into the two types non-proliferative & proliferative types.

NON-Proliferative

(a) EXCUDATES
(b) MACULAR EDEMA
(c) MICROANEURYSM
(d) HAEMORRHAGES

PROLIFERATIVE

(a) BLOOD VESSELS ABNORMALITIES

CAUSES OF THE RETINOPATHY

High levels of blood sugar block the tiny blood vessels in the retina, which is in the back of the eye. To compensate for the loss of blood supply, the eye develops new vessels. These do not function well and cause leakage of blood leading to vision problems.

SYMPTOMS

At the starting there is no symptoms observed, but after that it show some symptom like,
Poorly controlled blood sugar in diabetics
The risk increases with:

a) Duration of diabetes
b) High blood pressure
c) High cholesterol
d) Pregnancy
e) Tobacco use

PREVENTION

The following measures help prevent complications of diabetes such as diabetic retinopathy:
Modify your diet so as to control the blood sugar levels
Attend annual eye screening
Avoid tobacco and alcohol
Pay attention to any visual changes
Treat hypertension
Lose weight
Exercise regularly

COMPLICATIONS

Blindness
Vitreous haemorrhage
Retinal detachment

Glaucoma

2. NEPHROPATHY

Diabetic nephropathy is a serious kidney-related complication of type 1 diabetes and type 2 diabetes. It is also called diabetic kidney disease. About 25% of people with diabetes eventually develop kidney disease.Diabetic nephropathy affects your kidneys' ability to do their usual work of removing waste products and extra fluid from your body. The best way to prevent or delay diabetic nephropathy is by maintaining a healthy lifestyle and treating your diabetes and high blood pressure.

Over many years, the condition slowly damages your kidneys' delicate filtering system. Early treatment may prevent or slow the disease's progress and reduce the chance of complications.

Your kidney disease may progress to kidney failure, also called end-stage kidney disease. Kidney failure is a life-threatening condition. At this stage your treatment options are dialysis or a kidney transplant.

Clinically, it ischaracterized by the development of proteinuria with a subsequent decline in glomerular filtration rate, which progresses over a long period of time, often over 10–20 years.If left untreated, the resulting uraemia is fatal. Importantly, kidney disease is also a major risk factor for thedevelopment of macrovascular complications such as heart attacks and strokes. Hypertensionand poor glycaemic control frequently precede overt diabetic nephropathy, although a subset of patients develop nephropathy despite good glycaemic controland normal blood pressure. Once nephropathy is established, blood pressure isoften seen to rise, but paradoxically in the short term, therecan be improvements in glycaemic control as a result of reduced renal insulin clearance by the kidney.

The development and progression of nephropathy is highlycomplex given the diversity of cell populations presentwithin the kidney and the various physiological roles of thisorgan. Indeed, aside from the filtration of toxins from theblood for excretion, it is difficult to pinpoint which other

functional aspects of the kidney are most affected by diabetes. These include the release of hormones such as erythropoietin, activation of vitamin D, and acute control ofhypoglycaemia, in addition to maintenance of fluid balance and blood pressure via salt reabsorption. Highglucose

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concentrations induce specific cellular effects,which affect various resident kidney cells including endothelial cells, smooth muscle cells, mesangial cells,podocytes, cells of the tubular and collecting duct system,and inflammatory cells and myofibroblasts.

Currently utilized therapies to treat diabetic renal diseaselargely target systemic blood pressure and/or intraglomerular hypertension. Applied the most widely are inwhich alter the renin-angiotensin system (RAS) which includes angiotensin converting enzyme (ACE) inhibitors and angiotensin II (ANG II) receptor antagonists which are considered first line therapies for diabetic nephropathy.

CAUSES OF DIABETI NEPHROPATHY

In people with diabetes, the nephrons slowly thicken and become scarred over time. The nephrons begin to leak and protein (albumin) passes into the urine. This damage can happen years before any symptoms begin.

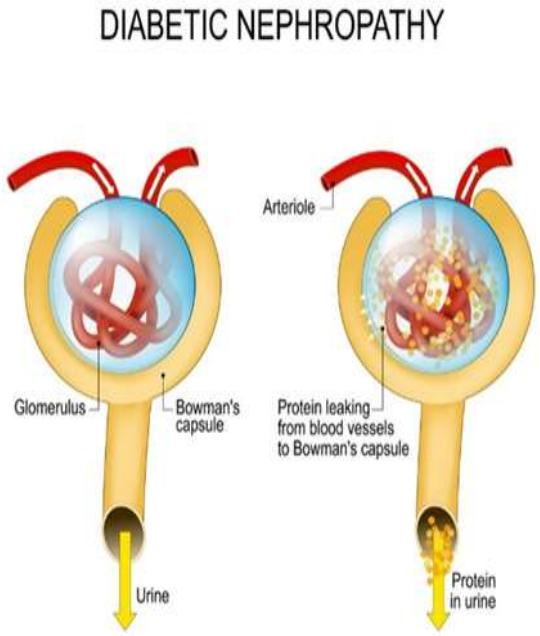

fig. represent the diabetic nephropathy.

SYMPTOMS

You may have symptoms if your nephropathy gets worse. These symptoms include:

Swelling (edema), first in the feet and legs and later throughout your body.
Poor appetite.
Weight loss.
Weakness.
Feeling tired or worn out.
Nausea or vomiting.
Trouble sleeping.

Screening

Most of the guidelines say that the screening of diabetic nephropathy is done by using the albumin/creatinine ratio ACR < 30mg/g creatinine.

This is coupled with the renal assessment and collaborated with the glomerular filtration rate.for the screening of nephropathy it staert immediate after detection of type-II diabetes & 5 years after type-I diabetes.

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Fig. represent the healthy kidney.

3.HEART DISEASE

Heart disease is the condition that affect the person with the diabetes, its worse the condition when it stays for longer time.Now-a-day the heart disease or the coronary heart disease is the major kill to mankind & 80% cases are deal with it.The people who suffering from type-I & type -II diabetes are more prone to the heart attack,stroke, and high blood pressure.In most of the cases person suffer from angina, myocardial infraction, heart diseases.

The high blood sugar increases the risk of complication of heart diseases.

This review, say that there is the strong link between the diabetes and heart diseases. The people with the diabetes are more prone to the heart risk than the normal people.

The heart disease & the stroke are leading cause of death, people with the diabetes as per the national institute of diabetes.

As per the survey, this review says that adult with the diabetes is more likely to die with the heart diseases than the diabetes.Due to the high sugar level, it damages the blood vessels, inflammation to the blood vessel, that it disrupts the flow flow through the vessel to the heart.

Therefore, it is important the people with diabetes should maintain their healthy diet and avoid excessive intake of food.And also do the regular cardio exercises.

LINK BETWEEN THE DIABTESES AND HEART RISKS.

1. Having high blood pressure = The both diabetes & the hypertension increases the risk of heart diseases.
2. Having unhealthy cholesterol and uncontrolled tri-glyceride level= thiscontributes to build-up of plaque in the arteries that resist the insulin.
3. Having obesity & body mass index over 30 = the weight loss with the people having diabetes and obesity effect to increases the insulin sensitivity.
4. Not getting enough physical exercise= the physical exercise can reduce the risk of cardiac failure, but in proper time to deal with it.

V. CONCLUSION

This review study is done to modernize the concept of diabetes and their complications. This topic also confirmed the importance of review related to the diabetes and their complication. Along with its complication it also presented with its cellular secondary messenger mechanism. Worldwideabout 80-90% people are suffered from the diabetes and their complications. A broad range of people living with the diabetes, we anticipate this review and the ongoing work on this topic will contribute to the development of targeted intervention better aligned with improving the health and well-being of people whose life are touched by diabetes.

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