

# An Overview of Diabetes Mellitus and Its Complications

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## Abstract

Diabetes is an emerging chronic disorder in present and future years. Diabetes is of two types type 1 and type II. In 2019, there were 9.3% adults were affected with diabetes and by an estimation studies by 2045 we will have around 700 million people living with the diabetes. In further years the risk of men affecting to diabetes will increase when compared to the women. The complications of the diabetes are much riskier when compared to the actual cause that is diabetes. The high blood sugar levels in the body will cause internal organ dysfunctions which may also lead to the organ failure. The main complications caused by the diabetes patients are diabetic retinopathy, diabetic nephropathy, diabetic neuropathy and diabetic cardio vascular diseases like diabetic cardio myopathy. In this present review article, the 40 articles were reviewed and has parts of diabetic complications and their diagnosis, management and treatments. The diabetic foods to include in the daily life to avoid further complications of the diabetes patients.

**Keywords:** Diabetes • Diabetic complications • Diabetic food

## Introduction

Diabetes is a chronic disorder that is characterized by increased glucose levels in the blood due to abnormalities in the insulin secretion and functions. Insulin is the important hormone for the conversion of blood glucose into energy. Absence of insulin in the body will increase the blood glucose levels in the body and causes Hyperglycaemia. If untreated the blood glucose levels increases and causes organ damages [1].

Diabetes is characterized by increased glucose levels due to defects in insulin release and mechanism. Diabetes is group of metabolic abnormalities of carbohydrates, fats and proteins. Diabetes mellitus is of mainly classified into 3 types Type-1 diabetes, Type-2 Diabetes. Diabetes severity is based on type and time period of diabetes [2].

Type-1 Diabetes is mainly caused due to the immune mediated mechanism and due to destruction pancreatic beta cells. The main symptoms of Type 1 diabetes are increased thirst (polydipsia), increased frequency of urination (polyuria), polyphagia (increased hunger). The replacement of endogenous insulin with exogenous insulin can manage the conditions of diabetes [3].

Type-2 Diabetes is mainly characterized by the insulin sensitivity, hyperglycaemia and known as non-insulin dependent diabetes. The main causes of Type 2 diabetes are lifestyle and environmental factors. These factors include physical inactivity, smoking, drinking alcohol and obesity [4].

Diabetes is a widely emerging epidemic. The complications of Diabetes are common in all types of diabetes. The chronic complications are divided into micro vascular and macro vascular. Micro vascular complications include nephropathy, neuropathy and retinopathy whereas macrovascular complications include cardiovascular complications [5].

## Pharmacoepidemiology of Diabetes

According to diabetes atlas 9.3 % of present world that is 463.0 million adults of age between 20-79 years have diabetes. Based on estimation studies done on 2019, by 2030, 578.4 million and by 2045, 700.2 million will have diabetes. The risk of diabetes is low among adults age between 20-24 years

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**Received** 26 July, 2021; **Accepted** 30 July, 2021; **Published** 02 August, 2021,

and is lower in women of age 20-79 when compared to men. In 2019 about 17 million more men are affected with diabetes compared to men. The risk of diabetes is to be increased in both men and women in coming years [6].

## Prevalence of Diabetic Complications

According to national Health and Nutrition Examination survey, the risk of kidney complications (Diabetic Nephropathy) is more when compared to other complications. The number of complications with cardiovascular are more when compared to other diabetic associated complications [7]. This present article mainly focuses on all mostly occurring diabetic complications and includes 40 articles in total and has parts of diabetes pathophysiology and epidemiology, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiovascular complications.

## Diabetic Retinopathy

It is a condition where diabetic patient loss vision and cause blindness due to damage in the retina of the eye. If untreated diabetic retinopathy may lead to other complications like Diabetic Macular Edema, Retinal detachment, Neovascular glaucoma [8].

## Stages of Diabetic Retinopathy

- Stage 1 No Apparent Retinopathy.
- Stage 2 Mild Non-proliferative Retinopathy.
- Stage 3 Moderate Non-proliferative Retinopathy.
- Stage 4 Severe Non-proliferative Retinopathy.
- Stage 5 Proliferative Diabetic Retinopathy [9].

## Pathology

The pathology of diabetic retinopathy is due to Hyperglycemia and retinal micro vasculopathy. Due to hyperglycemic condition in the blood vessels of the retina the blood vessels dilates and also losses pericytes These changes in the retina causes back flow of the blood and loss of structural support to the capillaries respectively causing diabetic retinopathy.

## Inflammation

Diabetic retinopathy can also be caused due to the inflammation [10]. Leukostasis is an important event in diabetic retinopathy pathogenesis, leading to capillary occlusion and ROS-mediated cell death, as well as amplifying the inflammatory response locally in the retinal tissue [11].

## Diagnosis

- Fluorescein angiography.
- Optical coherence tomography.

## Treatment of Diabetic Retinopathy

First treatment of diabetic retinopathy is the self-care that is to manage the blood glucose levels and blood pressure. Anti-Vascular Endothelial Growth Factor like bevacizumab (Avastin), ranibizumab (Lucentis), aflibercept (Eylea): Laser surgery; Vitrectomy [12].

## Diabetic Neuropathy

Neuropathy is a condition caused due to the damage, injury or compression of the nerves resulting in tingling, pain, altered sensations.

Neuropathy is of 4 stages they are as follows

Stage 1 Numbness and pain

Stage 2 Constant pain

Stage 3 Intense pain

Stage 4 Loss of sensation and complete numbness [13].

Diabetic neuropathy is mainly of 4 types

Peripheral Neuropathy/Diabetic Nerve Pain/Distal Polyneuropathy

Proximal Neuropathy (Diabetic Amyotrophy)

Autonomic Neuropathy

Focal Neuropathy

## Peripheral Neuropathy

Peripheral nerves are the nerves which are located outside the brain and spinal cord [14,15]. It includes 43 pairs of sensory and motor nerves which connects central nervous system to the body. This peripheral nervous system controls the functions like pain, movement, sensations. The damage to these peripheral nerves is known as peripheral neuropathy [16].

**Proximal neuropathy:** Proximal diabetic neuropathy is a rare type neuropathy caused when there is damage in nerves locates at hip, buttocks, Thighs. This type of neuropathy mostly affects one side of the body [17].

**Autonomic Neuropathy** is a group of symptoms that occur when there is damage to the nerves that manage every day body functions [18] and the nerves that control internal organs [19]. Autonomic neuropathy can cause damages to other systems like cardiovascular disorders (resting tachycardia, orthostatic hypotension) gastrointestinal tract (constipation, diarrhea) metabolic disorders(hypoglycemia) [20]. Focal Neuropathy is the result of damage to peripheral nerve at the one site. This type of neuropathy mainly occurs at a particular site/location near to the bone and across the joints.

## Causes for Focal neuropathy (nerve injuries)

External damage like trauma, external compression of nerves, cold burns, radiations

Internal entrapment or compression like compressions due to tumors, vascular malformations

Intrinsic lesion like infract of the nerves

Increased susceptibility to nerve injury due to underlying diseases like diabetes (Table 1) [21].

## Diabetics and Cardiovascular Diseases

High glucose levels in the body lead to the damage of the blood vessels and the nerves of the heart. The following heart conditions with the combination of high blood glucose levels may increase the risk of diabetic cardiovascular diseases. The risk factors include High blood pressure, High triglyceride levels, High low-density cholesterol [22-26]. Patients with diabetes already have an altered endothelial function which may lead to higher risk of atherosclerosis [27].

## Cardiac Myopathy

Diabetic cardiomyopathy is the abnormal functioning and structure of the myocardium in individuals with diabetes. The pathophysiology includes increased blood sugar levels, insulin resistance and increased insulin levels in the body will lead to the metabolic disorders and cardiac insulin resistance. These conditions may lead to other conditions like mitochondria dysfunction, inflammation, and autonomic neuropathy and these conditions may cause cardiac stiffness, hypertrophy and fibrosis causing cardiac diastolic, systolic dysfunction and Heart failure [28,29].

The other Risk factors that lead to Mitochondrial Effects are Smoking, Vasoactive agents (adrenaline, dopamine) will cause Mitochondrial dysfunction in cardiomyocytes, oxidative stress in vascular smooth muscles and endothelial cells will lead to atherosclerosis, and impaired ATP production with a calcium overload in mitochondria will lead to the aggravated hypertension. Hyperlipidaemia, hyperglycaemia and oxidized low density lipoprotein may lead to various cardiovascular problems [30].

The other cardiac complication is Cardiac-Diabetic Autonomic Neuropathy and has Signs and Symptoms of Resting tachycardia, Abnormal blood pressure, Orthostatic hypotension (weakness, faintness, visual impairment). The diagnostic tests include Beat to beat Heart Rate Variability, Diastolic blood pressure response to isometric exercise, Heart rate and systolic blood pressure to standing [31].

## Diabetic Nephropathy

In 2010 Diabetic nephropathy term was replaced with the diabetic kidney disease to explain the kidney damage than the changes in the Glomerular Filtration Rate. There are two types of staging of diabetic nephropathy based on the GFR rate and Kidney damage (Table 2) [32,33].

The common risk factors for the diabetic nephropathy are hyperglycaemia, hypertension, insulin resistance and other risk factor according to gender is smoking of cigar. The pathophysiology involves the increased levels of blood sugar levels will lead to increased levels of advanced glycosylation end products and will stimulate the intrinsic glomerular cells to produce TGF- $\alpha$  Cells which causes glomerular sclerosis and tubulointerstitial damage [34]. The screening parameter for nephropathy is detection of microalbuminuria determining urinary albumin/creatinine ratio (ACR), albumin excretion rate (AER) [35].

Diabetic nephropathy progression can be managed by controlling metabolic and haemodynamic abnormalities. Anti-hypertensive drugs along with hypoglycaemics can be used to manage the diabetic nephropathy (Table 3) [36].

## Other Complications

### Diabetic Foot

Due to underlying causes like peripheral neuropathy and ischemic conditions results in diabetic foot [37].

### Diabetic Encephalopathy

Hyperglycaemia and impaired insulin signalling can cause neuronal damage and neurodegenerative events and causes brain inflammation and neuronal death.

### Diabetic foods

Blood sugar levels can be better controlled by the diet. Foods that are lower in saturated fats, added sugars, and sodium has to be preferred. According to the American Diabetes Association the best choice of foods include Apples, blueberries, mushrooms, carrots, broccoli, onions, peppers, fat-free milk, millets, brown and wild rice, tomatoes, olives, almonds, lean meats, flaxseeds, sunflower seeds. Cut back soda, sugar foods and drinks, bad fats (dairy, butter), fried foods [37].

**Table 1:** Treatment for Neuropathy.

S no	Drug Class	Drug Name	Dose	Frequency	MAX Dose
1	Gabapentonooids	Gabapentin	Up to 600 mg	TID	3600 mg
		pregabalin	150 mg	BD or TID	600 mg
	Tricyclic anti-depressants	nortriptyline	10-25 mg	OD (night time)	150 mg
		amitriptyline	10-25 mg	QHS	150 mg
	Topicals	5% lidocaine	Apply the ointment to the pain area.		
		8% lidocaine			
	Serotonin and norepinephrine reuptake inhibitors	Duloxetine	30 mg	OD	225 mg
		venlafaxine	37.5 mg	OD	150 mg
	Combination therapy	Gabapentonooids +	Same as of individual doses		
		Tricyclic Anti-Depressants			
	opioids	Tramadol	50 mg	BD or QID	400 mg
		Morphine	50 mg	BD or QID	400 mg
	Anti-Convulsant	Valproate	250 mg	BD	1500 mg <sup>[22]</sup>
	Vitamins	Vitamin B12 <sup>[23]</sup>	1 mg	OD	
Vitamin D <sup>[24]</sup>		60,000 IU	Every week for 20 weeks		

**Table 2:** The classification of Diabetic Nephropathy according to Kidney Damage.

Class	Description
I	Mild or non-specific
Ila	Mild mesangial expansion
Ilb	Severe mesangial expansion
III	Nodular Sclerosis
IV	Advanced diabetic glomerulosclerosis

**Table 3:** The classification of Diabetes according to GFR.

Stages	Clinical Signs and Symptoms	Duration
I	GFR is normal or increased	May last for 5 years from the start of diabetes
	Renal plasma flow increased by 10-15%	
II	Normal GFR	Starts more or less 2 years after onset of diabetes
	With no clinical signs May have thickening of the basement membrane and mesangial proliferation	
III	Glomerular damage and microalbuminuria (30-300 mg/day) May have hypertension	5 – 10 years after onset of the diabetes
IV	GFR decreased below 60 ML/min	
	Chronic Kidney Disease with Irreversible Proteinuria (>300 mg/day) with a sustained hypertension	
V	End stage kidney disease with a glomerular filtration rate of <15 mL/min	

## Conclusion

According to reviewed articles diabetes is a chronic disorder which is caused due to an abnormal functioning of pancreas leading to decreased release of the insulin. Abnormal release of glucose will cause increased blood glucose levels in the body. Diabetes will lead to different complications like diabetic retinopathy, diabetic neuropathy, diabetic cardiac myopathy. Diabetes patients has to maintain blood glucose levels and has to maintain good diet to avoid further complications.

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**How to cite this article:** Sai Akhila, B. "An Overview of Diabetes Mellitus and Its Complications". *J Diabetic Complications Med* 6 (2021):154.