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REVIEW ARTICLE

TYPE 2 DIABETES MELLITUS: A REVIEW OF COMPLICATIONS, COMMON PATHWAYS AND ROLE OF PHARMACIST IN PATIENT COUNSELING

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ABSTRACT

Diabetes Mellitus is a group of metabolic diseases in which defects in insulin secretion or action result in elevated blood glucose. It is a major public health issue that affects over 285 million people globally. Diabetes is sighted as one of the leading causes of blindness, kidney failure, cardiovascular events and lower limb. Data from the United Kingdom Prospective Diabetes Study (UKPDS) and the Diabetes Control and Complications Trial (DCCT) shows that controlling hyperglycemia is critical for the reduction of negative clinical outcomes in diabetic patients. AGEs, oxidative stress, low grade inflammation and neovascularization of vasa vasorum paves the way for developing diabetic complications. The aim of the article is to review the published studies that examine the complications of Type 2 diabetes and the role of pharmacists on diabetes prevention and care. Pharmacists should identify the patients having diabetes and patient education should be provided. Humanistic outcomes like quality of life must also be taken into account while considering the clinical outcomes of the diabetes patients.

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INTRODUCTION

Diabetes is a progressive disease marked by hyperglycemia which is caused by abnormalities in insulin secretion, insulin action or both. [2]It is a serious disease that can cause complications such as blindness, kidney failure, heart attacks and strokes. It is a leading cause of lower limb amputations in the United States and fourth greatest cause of disease-related death .The pathogenesis of diabetic complication include certain genetic and epigenetic modifications as well as the nutritional status and increase the risk of occurrence in people leading sedentary life.[12] Classic symptoms of diabetes include polydipsia, polyuria, polyphagia, blurring of vision, thirst and weight loss.[1][13]The large amount of glucose in the blood causes an increase in serum concentration, or osmolality. High blood glucose may also cause fatigue, blurred vision, abdominal pain and headaches. Diabetes mellitus can either be Type 1 or Type 2. Type 1 diabetes, formerly called juvenile diabetes or insulin dependent diabetes, is caused by destruction of beta cells in the islets of Langerhans of the pancreas.

In Type 2 diabetes (formerly called adult-onset diabetes or non-insulin dependent diabetes mellitus), tissues are resistant to insulin. Another type of diabetes is gestational diabetes which arises during pregnancy. The pathogenic process associated with diabetes mellitus which includes the insulin resistance and the beta cell destruction are more rapidly seen in the youth onset type 2 diabetes than the adult patients.[3] A person with diabetes is at risk for a variety of complications. Acute complications such as hyperglycemia, hypoglycemia, diabetic ketoacidosis and hyperosmolar hyperglycemia are treatable and can often be prevented with appropriate care. Over time, chronic hyperglycemia causes a variety of serious complications in persons with diabetes and they can be micro vascular or macro vascular. Retinopathy, neuropathy, and nephropathy are micro vascular complications whereas coronary artery disease, peripheral vascular disease, and cerebrovascular events are the macro vascular complications.[1][13] The studies show that India claims number one position in diabetes population in the chart with 50.8 million diabetics.[13]

Patients with diabetes must have the knowledge to do their self-care activities confidently. Pharmacists can help to detect the diabetic patients through screening and should focus on those who are at risk. The purpose of this article is to review the published studies that evaluate the complications of diabetes and the impact of pharmacists in diabetes management.

DIABETES MELLITUS

Diabetes is a metabolic disorder in which the body's capacity to utilize glucose, fat, and protein is disturbed due to impairment in insulin secretion and or insulin resistance leading to chronic hyperglycemia.

Types of diabetes

Type 1 diabetes
Type 2 diabetes
Gestational Diabetes

Type 1 diabetes

Immune mediated diabetes: This type of diabetes, which affects only people who have diabetes and was previously known as insulin-dependent diabetes, type 1 diabetes, or juvenile onset diabetes, is caused by a cellular-mediated autoimmune destruction of pancreatic B cells.

Idiopathic diabetes: The causes of several types of type 1 diabetes are unknown. This kind of diabetes is highly hereditary, has no immunological evidence of B cell autoimmunity, and is unrelated to HLA.

Type 2 diabetes

This type of diabetes, which affects 90-95 percent of people with diabetes and was previously known as non-insulin dependent diabetes, type 2 diabetes, or adult-onset diabetes, encompasses people who have insulin resistance and, at least initially, and often throughout their lives, have relative insulin deficiency. These people do not require insulin treatment to live.[5]

Gestational diabetes

It's a disorder marked by an increased amount of glucose in the bloodstream during pregnancy that usually goes away once the baby is born.

DIABETIC COMPLICATIONS

If the blood sugar level is not controlled, there can be 2 types of complications.

- Acute (occurs suddenly)
- Chronic (occurs as long-term effect)

Acute Complications:

- Hyperglycemia
- Hypoglycemia
- Diabetic ketoacidosis
- Hyperosmolar hyperglycemic state

Chronic complications:

Microvascular Complications

- Diabetic Neuropathy
- Diabetic Nephropathy
- Diabetic Retinopathy

Macrovascular Complications

- Coronary Artery Disease (CAD)
- Peripheral Vascular Disease (PVD)
- CerebroVascular Disease (CVD)

COMMON PATHWAYS FOR DEVELOPMENT OF BOTH MICRO AND MACROVASCULAR COMPLICATIONS

- Advanced glycation products
- Oxidative stress
- Low grade inflammation
- Neovascularization of vasa vasorum

Advanced glycation end products: Advanced glycation end products (AGEs) are a diverse set of molecules generated by non-enzymatic glycation of plasma proteins that impair their normal function by modifying their molecular shape, disturbing enzyme activity, and interfering with receptor function. Advanced glycation end products build up in various types of cells, affecting their extracellular and intracellular structure and function by cross-linking with proteins, lipids, and nucleic acids, resulting in a range of diabetic problems.[14]

Oxidative stress: It is caused by the overproduction of reactive oxygen species, which plays a key role in the activation of other diabetic complications-related pathways like elevated polyol pathway activity, non-enzymatic glycation, and PKC levels, that all contribute to the development of micro and macro complications.[7][20]

Low -grade inflammation: Inflammation has been identified as a significant risk factor for both atherosclerosis and type 2 diabetes. In response to hyperglycemia, vascular cells undergo a number of early pathogenic alterations, including the loss of non-adhesive properties and monocyte adherence to endothelial cells, which is an early step in atherogenesis. Hyperglycemia has been shown to promote monocyte adherence to endothelial cells in the arteries. Hyperglycemia and advanced glycation end products have been linked to oxidative stress because both can induce the production of superoxide by endothelial cells.[8]

Neovascularization of vasa vasorum: The expansion of the vasa vasorum is linked to an increase in plaque burden, which promotes atherosclerosis. Neovascularization results by the growth from both adventitial layer (outward) and arterial lumen (inward) towards intima. [7]

COMPLICATIONS

Acute Complications:

Hypoglycemia

Hypoglycemia is a condition in which your blood glucose level is lower than normal.

Common Causes:

- Not eating enough
- Taking too much diabetic medication or insulin
- Drinking alcohol

Symptoms*:*

- Increased heart rate
- Excess sweating
- Blurred vision

Diabetic ketoacidosis

Hyperglycemia, ketosis, and metabolic acidosis are all symptoms. It is caused by a lack of absolute or relative insulin, which causes glucose dysregulation and the release of counter-regulatory hormones such as catecholamine, glucagon, and cortisol. Lipolysis is a normal metabolic process that goes awry in DKA, resulting in the generation of serum free fatty acids, which are used to make massive ketone bodies. (3 hydroxybutyrate, acetoacetate and acetone)[1]

Symptoms*:*

- Thirst
- Palpitation
- Abdominal pain

Hyperosmolar hyperglycemic state

Hyperosmolar hyperglycemic state is a significant diabetes related complication. It occurs when a person's blood glucose levels are abnormally high for an extended period of time, resulting in severe dehydration (great thirst) and confusion. [1]

Symptoms:

- Increased blood sugar level (Over 600 mg/dl)
- Confusion, hallucinations, drowsiness
- Dry mouth or extreme thirst that may get eventually better
- Fever over 100 °F
- Blurred vision
- Weakness or paralysis

Chronic complications:

Hyperglycemia is a condition in which the blood sugar level is too high. If this goes unchecked for 10-15 years, organ damage can occur.

It is of 2 types:

Microvascular Diseases

- Diabetic Neuropathy
- Diabetic Nephropathy
- Diabetic Retinopathy

Macrovascular diseases

- Coronary artery diseases
- Peripheral vascular diseases
- Cerebrovascular disease

Microvascular diseases

Diabetic neuropathy

It's a type of nerve damage that develops as a result of diabetes. The legs and feet are the most commonly affected areas.

It can be classified into 2;

- Symmetrical
- Asymmetrical

Asymmetrical form can be sensory, motor, or both, as well as affecting the particular cranial or peripheral nerves, whereas symmetrical form is predominantly sensory and autonomic.

Autonomic neuropathy

When the nerves that govern involuntary body functions are destroyed, this condition develops. Cardiac autonomic neuropathy can cause generalized weakness, light-headedness, or syncope, as well as tachycardia or bradycardia. [6]

Diabetic foot

It can happen when high blood sugar damages the nerves and blood vessels in the feet.

Symptoms:

- Swelling in foot
- Changes in skin color
- Pain in legs
- Open sores on the foot that are slow to heal

Diabetic nephropathy

It is the most common cause of chronic renal failure, the initial marker being microalbuminuria, which can be screened by measurement of albumin to creatinine ratio in a random spot collection.[4][5]

Symptoms

- Worsening of blood pressure control
- Increased need to urinate
- Protein in urine
- Swelling of feet and ankle

Diabetic retinopathy

Diabetic retinopathy is a long-term complication of diabetes that can cause vision loss. It develops as a result of high glucose levels in the retina's small blood vessels, causing abnormalities in the eye.[5]

Proliferative retinopathy

It is a developed form of retinopathy in which new, but weak blood vessels develop on the retina to assist restore blood flow. It is the body's attempt to save its retina, but it can induce retinal scarring and blindness.[11]

Diabetic macular edema

Macular edema is defined as thickening of the retina or the presence of hard exudates in the macula at two-disc diameters. In diabetic patients, the most common cause of significant vision loss is disc.

Diabetic papillopathy

Diabetic papillopathy is a very uncommon ocular symptom of diabetes. Unilateral or bilateral disc swelling with minimal or no optic nerve impairment is a sign of diabetes.

Macrovascular diseases

Coronary artery diseases

It occurs due to damage in the heart's major blood vessels due to the buildup of plaque. As a result, coronary arteries narrow and reduce blood flow to the heart.

Peripheral vascular diseases

It is also known as peripheral arterial disease is an occlusive disease of the large peripheral arteries especially of the legs which excludes the coronary and intracranial vessels, which are the mainly caused by atherosclerosis. [13]

Cerebrovascular diseases

Transient ischemic attack and stroke are three times more common in diabetic population than others. When comparing the mortality rate with non-diabetic population the levels of disability and the mortality rate has increased in those with diabetes after a stroke.[13]

ROLE OF PATIENT COUNSELING IN MANAGEMENT OF DIABETIC COMPLICATIONS

Diabetes has been more common in India during the last decade. Diabetic individuals develop complications as a result of a lack of knowledge about the condition and poor glycemic management. Patient education is the cornerstone of diabetes care and the most effective strategy to reduce diabetic complications and control the disease. Diabetic patients had an appropriate degree of knowledge, despite lack in some areas, and a good attitude towards their condition; there was a positive association between knowledge and attitude. The knowledge and practice responses, on the other hand, had no correlation. It was also discovered that a variety of factors other than knowledge and attitude play a role in disease management. Poor self-management, a lack of desire, a lack of social support, or a lack of resources that are required for long-term lifestyle change are all possible factors. The pharmacist's role in the management of chronic illnesses is becoming increasingly important in both the UK and the US. The community pharmacist is increasingly being regarded as the first choice of call for people seeking guidance on how to manage their disease.[10]Pharmacists played an important role in lowering modifiable vascular risk factors such as blood pressure and glycemic management. The information regarding drug route of administration, dose, frequency, intended use in specific population, etiology, risk factors, complications, clinical management, lifestyle and dietary modifications can be provided through oral/written or using counseling aids. [15] A significant association has been found between medication adherence and optimal glycemic control. Certain conditions such as memory impairment, growing age, social deprivation, co-morbidities and complex treatment regimen may act as hurdles in medication adherence. [19]Glycemic control improved even after critical demographic variables were adjusted and pharmacotherapy was intensified, indicating that pharmacist engagement had a favorable impact on medication adherence and other parameters that are crucial in diabetes self-care. Patients at high risk, persons with a family history of the condition, and mothers with a history of gestational diabetes or who delivered a baby weighing more than nine pounds should all be targeted for diabetes screening by pharmacists.

Patient education should begin soon after diagnosis, followed by a second stage in which a patient assessment can be completed, and a third stage in which patients can get information and education to reinforce concepts and provide motivation. [17] By providing people with diabetes with programs for monitoring therapeutic interventions and improving medicine compliance, as well as counseling on lifestyle factors to improve their quality of life, community pharmacists have the opportunity to play a critical role in managing diabetes and its complications. Several studies have reported that the patients following the diabetic education provided by a clinical pharmacist have an excellent quality of life. [9][15] In clinics, pharmacists were not directly involved in diabetic patient care. Doctors and nurses were in charge of diabetic patients. But in many cases the patients especially the newly diagnosed are often overwhelmed by the diagnosis and they have a poor understanding about the management and sometimes, the general practitioner also fails to provide adequate education regarding oral hypoglycemics and this can be overcome by a community pharmacist. Moreover the patients with poorly managed diabetes, that is those having HbA1c >9 mmol/L can also gain benefits from the pharmacist interventions, suggesting the appropriate targets the patient would likely to have. [16] Hospital pharmacists were primarily responsible for the acquisition and storage of anti-diabetics. On the other hand, out of 58 pharmacists, 51 (88 percent) were involved in counseling patients about medication storage and use. Patients may not understand the function of pharmacists in diabetes management based on these findings. As a result, pharmacists must keep up to date on diabetes through seminars, continuing education, and professional development in order to participate effectively in diabetes management and patient care. [18]

CONCLUSION

If untreated, diabetes is a globally frequent disease that can progress to life threatening consequences. The review demonstrates that there are significant improvements in knowledge and self-care behaviors in diabetes patients. Patient counseling plays an inevitable role in maintaining patient medication adherence and lifestyle modifications. One of the major reasons for patient’s non compliance is lack of awareness on medications and routine checkups. So here comes the importance of pharmacists in lowering modifiable

vascular risk factors such as blood pressure and glycemic management. We conclude that, despite the burden of type 2 diabetes increasing, approaches are taken to identify pathways that lead to diabetes complications, to detect the high-risk patients. All these findings lead to adapt proper treatment measures and to minimize the serious effects of diabetes. Data of this review could be used to further study of complications and the role of clinical pharmacists on diabetes prevention.

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