REVIEW ARTICLE

Prescribing Pattern of Antidiabetic Drugs and Its Adherence to American Diabetes Association Guidelines in Patients of Type 2 Diabetes Mellitus with and Without Comorbidities

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ABSTRACT

Diabetes mellitus is a persistent metabolic illness defined by high amounts of glucose in the blood, and it presents a substantial worldwide health problem. The incidence of diabetes is escalating at a quick pace as a result of variables including urbanization, lack of exercise and changing dietary patterns, particularly in developing countries where undiagnosed cases are prevalent. This review examines the prescription patterns of antidiabetic drugs for type 2 diabetes mellitus patients (T2DM), both with and without comorbidities, and evaluates adherence to the American Diabetes Association (ADA) guidelines. Effective management of T2DM is critical to preventing complications, but poor medication adherence remains a significant issue, leading to adverse outcomes and high healthcare costs. This review analyzes commonly prescribed oral hypoglycemic agents, their mechanisms of action, and side effects and discusses the importance of managing T2DM to prevent microvascular and macrovascular complications.

Challenges in adhering to ADA guidelines include lack of awareness, physical and architectural barriers, effective communication, and financial constraints. Addressing these challenges through multidisciplinary care, continuous medical education, and comprehensive public health interventions is essential for improving patient outcomes and mitigating the global diabetes epidemic.

Keywords: Type 2 Diabetes Mellitus, Antidiabetic drugs, Prescription patterns, ADA guidelines.

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INTRODUCTION

Prescription Pattern Analysis in Diabetes Patients

Diabetes mellitus, an incurable physiological illness defined by increased blood glucose levels, has become an important international health issue due to its rapidly increasing epidemic. Diabetes impacted about 422 million persons worldwide in 2014 and is anticipated to increase further (Lović *et al*., 2020). The significant increase in diabetes prevalence is attributed to variables such as urbanization, lack of exercise, and changing dietary patterns.[1,2]

In developing economies, the issue is further compounded by the high percentage of undiagnosed diabetes cases, which can surpass 50% of the total affected population. This is primarily due to the less developed healthcare systems in these regions.[3]

The increasing incidence of diabetes presents a substantial burden on healthcare systems, as patients often suffer from multiple comorbidities that require comprehensive management. Fortunately, the availability of various. Medications that lower glucose, cholesterol, and blood pressure can greatly reduce the chances of both macrovascular and microvascular problems linked to diabetes. However, the success of this outpatient management approach is heavily dependent on patient adherence to the prescribed medication regimen.[4]

Studies have shown that poor medication adherence is a significant challenge in diabetes management, contributing to adverse clinical outcomes and increased healthcare costs. According to the World Health Organization, Insufficient compliance with long-term medicines significantly undermines the efficacy of treatment, making it a crucial concern in public health. In the United States alone, the estimated cost of non-adherence-related hospitalizations for diabetes has been estimated at $100 billion per year.[5]

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Global Alarming Situation of Diabetes Mellitus

Diabetes mellitus is a persistent metabolic condition marked by high amounts of glucose in the blood. has become a global health crisis of staggering proportions. The International Diabetes Federation reports that around 537 million adults had diabetes in 2021, with more than 75% of them residing in low- and middle-income countries. The projected figure for 2040 is estimated to reach 642 million, suggesting an increasing prevalence of the disease, especially in emerging countries.[6] Diabetes is a prominent global cause of mortality, accounting for around 5 million deaths in 2015 and an anticipated 6.7 million deaths in 2021.[7] The countries with the highest diabetes-related death rates worldwide are the People's Republic of China, India, the United States, and the Russian Federation. The rising occurrence of both type 1 and type 2 diabetes has raised the frequency of diabetic complications, which vary from sudden, life-threatening conditions to long-term, incapacitating complications that impact multiple organ systems, such as retinopathy, nephropathy, neuropathy, and cardiovascular disease.

The global burden of diabetes is not only measured in human lives but also in the staggering healthcare expenditures it incurs. In 2015, The global health expenditure linked to diabetes was predicted to be $673 billion, with 75% of these expenses allocated to low- and middle-income nations.

This escalating financial burden on healthcare systems further exacerbates the challenges of providing effective diabetes management and prevention strategies, especially in resource-constrained regions.[8]

The alarming global situation of diabetes mellitus underscores the urgent need for comprehensive public health interventions, improved access to quality healthcare, and the implementation of evidence-based strategies to address this growing epidemic. Strategies such as increased awareness, early diagnosis, effective management, and the promotion of healthy lifestyles can play an essential role in mitigating the devastating impact of diabetes worldwide. By addressing this global health crisis, we can endeavor to enhance the standard of living. For millions of individuals affected by this chronic condition and, reduce the significant social, financial, and healthcare system implications it poses.[9,10]

Pathophysiology of Diabetes Mellitus

Diabetes mellitus is a chronic metabolic disorder marked by the body's incapacity to effectively manage blood glucose levels. This disease is primarily characterized by elevated blood glucose levels resulting from inadequate insulin secretion by the pancreas or the body's peripheral tissues becoming resistant to insulin's actions.[11] People with diabetes mellitus have an increased susceptibility to experiencing a range of consequences, including cardiovascular disease, renal failure, and visual impairments. Type 1 diabetes is the result of an autoimmune process that destroys the beta cells in the pancreas responsible for making insulin, resulting in a complete lack of insulin. On the other hand, type 2 diabetes is characterized by insulin resistance and relative insulin deficiency. In addition to genetic predispositionLifestyle variables, including the consumption of high-calorie foods, being sedentary, and obesity, have a substantial impact on the onset of type 2 diabetes. Understanding the pathophysiology of diabetes mellitus is crucial for the development of effective treatments and preventive measures for this widespread and debilitating condition.[12]

The metabolic derangements associated with diabetes mellitus can lead to a variety of pathological effects. Chronic hyperglycemia, a hallmark of diabetes, can induce oxidative stress and inflammation within the body. This imbalance between radical formation and antioxidant defenses can lead to the progression of chronic condition complications like neuropathy, retinopathy, and nephropathy. Furthermore, the persistently high levels of glucose in the blood can damage the blood vessels, leading to macrovascular complications like coronary artery disease, peripheral vascular disease, and stroke.[13]

In addition to the direct effects of high blood glucose, diabetes mellitus also disrupts lipid metabolism, leading to dyslipidemia and an increased risk of atherosclerosis. The dysregulation of lipid levels, having high levels of triglycerides and low amounts of high-density lipoprotein cholesterol is a characteristic of a condition that increases the risk of cardiovascular problems in people with diabetes.[14]

Moreover, diabetes mellitus is associated with dysfunctions in various organ systems. The kidneys can be affected by diabetic nephropathy, leading to decreased kidney function and, ultimately, end-stage renal disease. The eyes are also susceptible to damage, as chronic hyperglycemia can lead to diabetic retinopathy and vision impairment.[15]

Understanding the complex interplay of these pathophysiological processes is crucial for the holistic management of diabetes mellitus. Targeted interventions aimed at controlling blood glucose levels, managing lipid abnormalities, and preserving organ function can help enhance the standard of living for those with diabetes and mitigate the risk of complications. Developing a comprehensive understanding of the pathophysiology of diabetes mellitus is essential for guiding therapeutic strategies and advancing research efforts toward more effective treatments and preventive measures. The following classes of oral hypoglycemic agents are commonly prescribed in Table 1.

Importance of Managing T2DM Effectively to Prevent Complications

T2DM is a long-term metabolic disorder marked by the body's ineffectiveness in utilizing insulin, a hormone that regulates blood sugar levels. The incidence of this ailment is substantial and it is steadily increasing due to the growing number of elderly individuals and the escalating rates of obesity worldwide. Diabetes has a significant impact on various organs, and problems arising from elevated blood glucose levels are a major contributor to disability, diminished characteristics of living, and untimely mortality. Indeed, it is projected that the worldwide occurrence of diabetes would surge by 65% inside

Table 1: Oral hypoglycaemic agents

Class	*Mechanism of action*	*Examples*	*Notable side effects*
Biguanides	Reduces the synthesis of glucose in the liver and enhances the body's response to insulin.	Metformin (Glucophage)	Gastrointestinal issues (e.g., diarrhea), lactic acidosis (rare)
Sulfonylureas	Stimulates insulin release from pancreatic beta cells	Glipizide (Glucotrol), Glyburide (Diabeta), Glimepiride (Amaryl)	Hypoglycemia, weight gain
Meglitinides	Stimulates rapid, short-term insulin release from pancreatic beta cells	Repaglinide (Prandin), Nateglinide (Starlix)	Hypoglycemia, weight gain
Thiazolidinediones (TZDs)	Increases insulin sensitivity in muscle and adipose tissue	Pioglitazone (Actos), Rosiglitazone (Avandia)	Weight gain, edema, risk of heart failure, bone fractures
Dipeptidyl peptidase-4 (DPP-4) inhibitors	Prevents DPP-4 enzyme, increasing incretin levels and insulin secretion	Sitagliptin (Januvia), Saxagliptin (Onglyza), Linagliptin (Tradjenta)	Nasopharyngitis, headache, pancreatitis (rare)
Sodium-glucose cotransporter-2 (SGLT-2) inhibitors	Decreases glucose reabsorption in the kidneys, increasing glucose excretion	Canagliflozin (Invokana), Dapagliflozin (Farxiga), Empagliflozin (Jardiance)	Genital infections, urinary tract infections, dehydration, ketoacidosis (rare)
Alpha-glucosidase inhibitors	Delays carbohydrate absorption in the intestine	Acarbose (Precose), Miglitol (Glyset)	Gastrointestinal issues (e.g., flatulence, diarrhea)
Bile acid sequestrants	Lowers blood glucose through unknown mechanisms	Colesevelam (Welchol)	Constipation, indigestion
Dopamine agonists	Modulates hypothalamic regulation of metabolism	Bromocriptine (Cycloset)	Nausea, dizziness, fatigue

the next two decades. The rising incidence rates of type 2 diabetes pose a significant worry for governments and health-insurance providers due to the higher occurrence of several comorbid illnesses among patients with this disease compared to those without it.[16]

Thankfully, the use of several drugs that can lower glucose, cholesterol, and blood pressure levels is an effective way to reduce the likelihood of developing macrovascular and/or microvascular issues. These medications are easily accessible and can be administered on an outpatient basis. The primary goals of treatment are to prevent both immediate and long-term consequences related to diabetes. Diabetes is an incurable disease that necessitates ongoing medical care and attention to address various risk factors and treatment strategies beyond simply controlling blood sugar levels.[17]

Worldwide in 2015, diabetes was responsible for the deaths of almost 5 million individuals aged 20 to 79, resulting in one death occurring every 6 seconds. Diabetes has two main types of long-term consequences: microvascular and macrovascular. Microvascular issues are more common than macrovascular complications.[18]

Microvascular problems encompass neuropathy, nephropathy, and retinopathy, whilst macrovascular complications comprise cardiovascular disease, stroke, and peripheral artery disease. Determining the frequency of diabetic complications is difficult due to the absence of globally accepted diagnostic standards.[19]

Aside from medical treatment, support and education for patients play crucial roles in effectively managing type 2 diabetes and avoiding its consequences. Therefore, these medications are advised for simultaneous use by average individuals, particularly those who are older or have several risk variables.[20]

Prescribing Patterns in T2DM without Comorbidities

Type 2 diabetes mellitus (T2DM) is a persistent metabolic disorder that impacts a significant number of people globally. It is defined by the presence of insulin resistance and decreased insulin production, resulting in high blood sugar levels. While type 2 diabetes is often related to comorbidities like as hypertension and dyslipidemia, a significant portion of patients do not present with additional medical conditions.[21,22] This research paper aims to investigate the commonly prescribed antidiabetic medications this study aims to examine the prescribing patterns in individuals with type 2 diabetes who do not have any other medical conditions and to compare these patterns with the guidelines established by the American Diabetes Association (ADA).

The frequency or occurrence of type 2 diabetes has been steadily increasing, with projections of a 65% rise in global prevalence over the next 20 years.[23] This trend is largely attributed to an aging population and the growing obesity epidemic.[24] Appropriate management of type 2 diabetes is crucial, as the condition is linked to increased death rates, elevated healthcare expenses, and diminished standard of life.

While treatment strategies have improved for conditions such as hypertension and dyslipidemia, achieving optimal glycemic control remains a challenge, with only 13.2% of individuals with diabetes meeting target levels for blood glucose, blood pressure, and cholesterol.[25]

Proper compliance with specified instructions for medications plays a critical role in regulating type 2 diabetes. Unfortunately, non-adherence is a widespread issue, with high prevalence among individuals with this chronic condition. Inadequate adherence to medicine is associated with insufficient control of blood sugar levels, elevated rates of illness and death, and greater expenses in healthcare. Factors influencing medication adherence include patient demographics, attitudes toward drugs and perceived effectiveness of treatment burden. Identifying and addressing these barriers to adherence is crucial for improving patient outcomes.[26]

Prescribing Patterns in T2DM with Comorbidities

Managing type 2 diabetes mellitus (T2DM) with comorbidities is a multifaceted and intricate process multifaceted challenge in clinical practice. Type 2 diabetes is a chronic disorder that frequently occurs alongside other health problems, including cardiovascular disease, kidney damage, and other conditions.[27]

Commonly Prescribed Antidiabetic Drugs in Patients with Specific Comorbidities

When selecting antidiabetic drugs for people with type 2 diabetes and unique needs, comorbidities are guided by various factors, including the drugs' mechanisms of action, safety profiles, and potential for managing the concurrent conditions. In patients with cardiovascular disease, medications that have been shown to have cardiovascular benefits, such as metformin, GLP-1 agonists, and SGLT-2 inhibitors, are often preferred.[28]

In addition to these medications, ACE inhibitors and ARBs may also be prescribed to manage blood pressure and minimize the likelihood of cardiovascular events in people who have both type 2 diabetes mellitus (T2DM) and coexisting cardiovascular illness. Healthcare providers must diligently evaluate the unique requirements of each patient and take into account the potential interactions between antidiabetic drugs and other medications used to manage comorbid conditions.[29]

When managing T2DM in patients with renal impairment, healthcare providers should adjust the dosages of antidiabetic medications based on the patient's renal function. For example, metformin should not be used in people with serious kidney damage since it can increase the likelihood of developing lactic acidosis, whereas other antidiabetic agents, such as DPP-4 inhibitors, may be preferable in this patient population.[30] Healthcare practitioners must prioritize staying informed about the most recent information and recommendations in order to effectively manage T2DM and its associated conditions. Collaborative care involving a multidisciplinary team is often necessary to tackle the complex requirements of individuals diagnosed with type 2 diabetes mellitus and comorbid conditions, with the objective of attaining glycemic regulation while minimizing the risk of adverse events and optimizing overall health outcomes.[31]

Adherence to ADA Guidelines

The American Diabetes Association (ADA) has released extensive guidelines for the management of type 2 diabetes outlining evidence-based recommendations for the prescription of antidiabetic drugs.[32]

However, studies have shown that adherence to these guidelines is often suboptimal, with a significant proportion of healthcare providers failing to follow the recommended treatment protocols.[33-35]

A review of the literature highlights the importance of adherence to ADA guidelines, as it is associated with Enhanced regulation of blood sugar levels, decreased incidences of complications associated with diabetes and improved overall patient outcomes. In addition, patient-related factors, including medication costs, complexity of the treatment regimen, and cultural beliefs, also play a significant role in adherence to ADA guidelines. Understanding these barriers is crucial in developing targeted interventions to improve adherence and patient outcomes.[36,37]

Furthermore, the impact of non-adherence to ADA guidelines on patient outcomes cannot be overlooked. Suboptimal Adherence has been linked to a higher rate of hospitalizations, higher healthcare costs, and poorer quality of life for patients with T2D. (Asche *et al.*, 2011) Moving forward, identifying effective strategies to enhance adherence to ADA guidelines, such as continuous medical education for healthcare providers, patient education and support programs, and the use of decision support tools, will be essential in improving the management of T2D and, ultimately, patient outcomes.[38]

Treatment with Insulin Injections

Insulin, an essential hormone secreted by the pancreas, has a crucial function in controlling blood glucose levels in the human body. Individuals afflicted with type 2 diabetes, which is distinguished by insulin resistance and elevated glucagon secretion, frequently require exogenous insulin to maintain proper glucose metabolism.[39,40] Without sufficient insulin, the body's cells are unable to absorb glucose, resulting in elevated levels of blood sugar. Insulin injections replicate the natural production of insulin by the pancreas, hence reducing blood sugar levels effectively.

When beginning insulin therapy, it is essential for individuals to learn the proper injection technique. This includes understanding how to measure the correct dosage, selecting the appropriate injection site, and ensuring sterile administration to prevent infections.[41]

Furthermore, it is crucial for individuals to closely monitor their blood glucose levels and take appropriate action as needed adjustments to their insulin dosage as directed by their healthcare provider. As part of a comprehensive treatment plan, incorporating a balanced diet and maintaining a consistent exercise routine is crucial for effectively controlling blood glucose levels. Managing diabetes with insulin injections requires a commitment to routine and continuous monitoring, but it can significantly improve overall health and enhance the overall well-being of those diagnosed with type 2 diabetes.[42]

Challenges and Barriers in Following ADA Guidelines

As the healthcare industry strives to provide equitable and accessible care, the implementation of the Americans with Disabilities Act (ADA) guidelines has become a crucial aspect of service delivery. However, the path to full compliance is fraught with various challenges and barriers that must be addressed.[43,44]

One of the major challenges in implementing ADA guidelines isthe absence of awareness and education and development within the healthcare industry staff. Many individuals may not fully understand the requirements of the ADA or how to effectively accommodate individuals with disabilities. As a result, there is a need for comprehensive training programs to educate healthcare providers on ADA guidelines and best practices for accommodating patients with diverse needs.[45]

Physical and Architectural Barriers

Another significant barrier in meeting ADA guidelines is the presence of physical and architectural barriers within healthcare facilities. These barriers can include inaccessible entrances, narrow hallways, and inadequate facilities for individuals with mobility impairments. Overcoming these obstacles often requires substantial renovations and investments in retrofitting existing structures to ensure accessibility for all patients.[46]

Effective communication and information access for patients with disabilities is another challenge that healthcare providers face in adhering to ADA guidelines. Ensuring that individuals with hearing, vision, or cognitive impairments have equal access to information about their care requires the utilization of alternative communication methods, such as sign language interpreters, accessible electronic health records, and other assistive technologies.[47]

Financial constraints present a significant barrier to the full implementation of ADA guidelines in healthcare settings. Meeting the requirements for accessibility often involves substantial costs, including the purchase of specialized equipment, architectural modifications, and ongoing staff training. Healthcare organizations may struggle to allocate the necessary resources to achieve and maintain compliance with ADA standards.

Addressing these challenges and barriers is essential to ensure that healthcare facilities can effectively meet the needs of all patients, regardless of their abilities. By prioritizing awareness, training, physical accessibility, and communication strategies, healthcare providers can work towards creating an inclusive and equitable care environment in accordance with ADA guidelines.[48,49]

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