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Review

Exploring Multitargets Treatment for Diabetes

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Abstract

Diabetes Mellitus (DM) is a degenerative disease that modifies the body's glucose metabolism. Although glucose is a vital energy source for body cells, individuals with diabetes can either not use insulin efficiently or do not create enough of this hormone, which controls blood sugar. This review aimed to explore the multi-target treatment for diabetes. This study investigates explicitly recent reports published in peer-reviewed journals indexed in various databases, including Web of Science, Scopus, PubMed, Google Scholar, and Science Direct. Individuals with diabetes are more likely to experience other health issues, such as elevated blood pressure and cholesterol. Environmental factors that can influence the onset of diabetes include air pollution, temperature and weather, and stress. With the shortage of diabetes specialists and healthcare experts coupled with an inefficient healthcare service in low- and middle-income nations, there is a need to introduce more creative approaches to treat diabetes. Although literature reveals that no one-size-fits-all

method is available for managing diabetes because each person's reaction to the disease varies depending on several factors, such as the diabetes stage and the person's susceptibility to complications, this study posits that there could be a headway in diabetes management by exploring multi-targets treatment. Introducing lifestyle change, diet modification and physical activity could reduce the risk of death due to diabetes. This study also highlights how diabetes can be managed in the rural and urban settings. Adopting telemedicine and web-based initiatives could impact diabetes treatment positively.

Keywords
Diabetes mellitus; multi-target treatment; lifestyle changes; environmental factors

1. Introduction

Diabetes Mellitus (DM) is a complicated, long-term condition marked by improper glucose uptake and storage by the body [1]. Lifetime care is necessary to prevent or postpone incapacitating complications or premature death. It has been proposed that the term "premature atherosclerosis with associated hyperglycemia" be used to describe diabetes, highlighting the clinical issues that the majority of patients experience [2]. According to estimates, the age-standardized prevalence of diabetes worldwide is 7.9% for women and 9.0% for men who are 18 years of age or older [3]. Currently, more than 400 million persons worldwide have diabetes, and in the next 25 years, this figure is predicted to rise by 50% [4]. This report is in sync with the estimates from the International Diabetes Federation (IDF), which states that there were 451 million diabetics globally in 2017 and 693 million will have the disease by 2045. Furthermore, it is reported that about 50% of DM patients go undiagnosed [5]. Severe consequences include stroke, myocardial infarction (MI, sometimes known as a "heart attack"), kidney failure, nerve damage, vision loss, and limb amputation as a result of poorly controlled diabetes. Complications related to diabetes not only lower a patient's quality of life but also have a financial burden on society as a whole, the patients, and their families. In 2017, the anticipated cost of healthcare associated with diabetes worldwide was over USD 700 billion, which is expected to rise over the next 25 years. This presents a significant challenge to many nations' resources and healthcare systems [5]. The cornerstones of managing diabetes are self-management, changes in lifestyle, and education. Diabetes management is complicated and necessitates ongoing monitoring, input from a multidisciplinary team, regular contact between patients and providers, and support from the community [3]. Although medication and lifestyle modifications can help achieve adequate glycaemic control, there is no one-size-fits-all method for managing diabetes. Each person's reaction to the disease varies depending on their projected lifespan, diabetes stage, duration, and susceptibility to complications. Given the high prevalence of diabetes and the shortage of diabetes specialists, creative approaches that use digital interventions can improve diabetes care as part of a multimodal strategy that adheres to proven treatment protocols. This is especially important for low- and middle-income nations where there is a severe lack of healthcare experts and a deficiency in healthcare services [4]. According to Diabetes UK research, just 6% of diabetic patients receive the required services, and less than half of those with the disease undergo routine

health examinations. Diabetes is becoming more and more common, making it clear that the current methods of treatment will not be able to meet the need for treatment in the future. As a result, inventive concepts are required to raise the effectiveness of the present healthcare systems [3].

2. Classification of Diabetes

The four major categories of diabetes mellitus are type 1 diabetes, type 2 diabetes, other specific types of diabetes, and gestational diabetes.

2.1 Type 1 Diabetes Mellitus (T1DM)

It is an autoimmune disease, a less frequent form of the disease [3]. Autoimmune inflammatory processes typically cause the destruction of pancreatic b-cells. Autoantibodies against islet cells, glutamic acid decarboxylase (GAD), insulin, tyrosine phosphatases IA-2 and IA-2b, and the zinc transporter ZnT8 are examples of serum autoimmune indicators. Although the rate of progression might vary, this damaging process usually results in absolute insulin insufficiency with undetected levels of plasma C-peptide [2].

2.2 Type 2 Diabetes (T2DM)

It is a complicated metabolic disease linked to b-cell malfunction brought on by either inadequate secretion or variable degrees of insulin resistance. In people with type 2 diabetes, resistance to insulin can also be present in other metabolic disorders such as obesity, polycystic ovarian syndrome, and hypertension [2, 3].

2.3 Gestational Diabetes (GDM)

This is described as a glucose intolerance that begins or is initially identified during pregnancy, with the exception of women who most likely have pre-gestational diabetes. Pregnancy-related medical complications like this one are prevalent and are linked to a higher risk of unfavorable outcomes. Despite the fact that the illness usually goes away after delivery, affected women should be counseled about their higher risk of type 2 diabetes in later life and evaluated for persistent diabetes after giving birth [6].

2.4 Less Common Types of Diabetes Mellitus

Numerous different kinds of diabetes have been genetically defined, although the genetic basis of type 2 diabetes is not entirely understood. Among them, the most prevalent kind is maturity-onset diabetes of the young (MODY), a hereditary form of the disease linked to mutations in specific hepatic or b-cell genes (such as glucokinase and HNF homeobox A (HNF-1a)). It is inherited dominantly through autosomes [2].

2.5 Other Well-Characterized Forms of Diabetes (Usually Called 'Secondary Diabetes')

They include pancreatic disease-related diabetes (such as diabetes linked to hemochromatosis), excesses of corticosteroids or other hormones, or specific medications (such as immune

checkpoint inhibitors used to treat cancer, protease inhibitors used to treat HIV infections, and atypical antipsychotics used to treat schizophrenia) [2].

3. What is Pre-Diabetes?

"Impaired glucose tolerance" (IGT) and "impaired fasting glucose" (IFG) are the terms used to describe the areas in between normal and overt diabetes. It has been suggested that these lower hyperglycemic states represent "pre-diabetes," although they are not clinical diseases. They are significant because they are potent predictors of the emergence of overt diabetes in the future [2].

4. Complications from Diabetes

Diabetes is linked to long-term harm to the body's macrovascular and microvascular systems, which are the terms for the major and minor blood arteries. While damage to the macrovascular system, such as the coronary and cerebrovascular arteries, is the primary cause of death for people with diabetes 2, harm to the microvascular network, which includes the kidney, nerves, and eyes, is much more common and also significantly affects death rates [1].

4.1 Diabetic Kidney Disease (DKD)

Diabetic kidney disease (DKD), also known as diabetic nephropathy, is a progressive illness characterized by reduced kidney function brought on by hyperglycemia, which frequently coexists with the presence of albumin in the urine. Non-specific kidney disease is a condition in which people with diabetes may also exhibit signs of impaired renal function due to risk factors such as overweight, dyslipidemia, or hypertension that are unrelated to or not dependent on their diabetes. While elevated albuminuria and reduced estimated glomerular filtration rate (eGFR) are the two leading clinical indicators used to diagnose DKD, the temporal correlation between the diagnosis of diabetes and the beginning of kidney disease can aid in differentiating between DKD that is specific to diabetes and DKD that is not [1]. Prolonged hyperglycemia, or elevated blood sugar levels linked to diabetes, is the leading cause of diabetic kidney disease (DKD). The kidneys' glomeruli, which are tiny blood arteries and filters, can be harmed by persistently high blood sugar levels, which can result in protein leakage and a reduction in filtration capacity. Poor glycemic control (high HbA1c levels), uncontrolled hypertension (high blood pressure), dyslipidemia (abnormal blood lipid levels), smoking, obesity, a family history of kidney disease, and prolonged duration of diabetes are risk factors for developing diabetic kidney disease (DKD) [7].

There are five phases of diabetic kidney disease (DKD), and each one is distinguished by particular alterations in kidney function and the presence of protein in the urine: Hyperfiltration: Increased glomerular filtration rate (GFR) without significant protein in the urine. Incipient nephropathy: Microalbuminuria (small amounts of protein in the urine) without a substantial decline in GFR. Overt nephropathy: Macroalbuminuria (large amounts of protein in the urine) and a decrease in GFR. Renal insufficiency: Reduced GFR and increased serum creatinine levels. End-stage renal disease (ESRD): Severely reduced GFR (less than 15 mL/min/1.73 m^2) requiring dialysis or kidney transplantation [8].

Early detection and prompt management of DKD are crucial to prevent or delay the progression of kidney damage and reduce the risk of cardiovascular complications and ESRD.

The most effective method for establishing this distinction is kidney biopsy, which is uncommonly obtained and rarely required for treating kidney disease. The difficulties in researching diabetes complications are mostly due to distinctions between diabetes-specific and non-specific DKD. There is currently no known cure for DKD; however, blood sugar control, proteinuria, and kidney destruction are managed till the disease reaches its advanced stages, at which point dialysis or a kidney transplant are usually required for survival. End-stage kidney disease (ESKD), which is linked to a higher death rate, is most frequently caused by DKD [1].

4.2 Diabetic Retinopathy

Hyperglycemia can cause the blood vessels in the retina to gradually deteriorate, which increases the risk of retinal detachment, bleeding, and loss of vision. Diabetic retinopathy can be divided into two types: the more severe, late-stage PDR form, which is defined by the proliferation of new, fragile, leaky blood vessels throughout the retina and into the vitreous, and the earlier, more frequent non-PDR form, which is characterized by weaker blood vessels. Direct macula damage, also known as clinically significant macular edema, is a unique kind of diabetic retinopathy. The most frequent complication of diabetes is diabetic retinopathy, which affects about 35% of people with the disease overall, with significant regional and ethnic variations. Moreover, the primary cause of adult blindness in the United States, Wales, and England is diabetic retinopathy. The length of diabetes, age at being diagnosed, blood pressure levels, insulin usage, and the prevalence of protein in urine are all related to the extent of diabetic retinopathy [1].

A dangerous side effect of diabetes that can cause blindness and vision loss is diabetic retinopathy. The little blood vessels in the retina, the light-sensitive tissue at the back of the eye, are harmed by high blood sugar concentrations. Weak blood sugar control, high blood pressure, high cholesterol, and the length of diabetes are risk factors for diabetic retinopathy. Since laser surgery and other therapies can frequently avoid visual loss if the problem is discovered early, early detection and treatment are essential. People with diabetes should have regular eye exams since diabetic retinopathy often has no early warning symptoms [9].

5. Macrovascular Complications

Although it is commonly known that people with diabetes have a higher risk of cardiovascular disease (CVD), people with diabetes have a two- to ten-fold higher likelihood of a cardiovascular event compared to people without diabetes, depending on the type of diabetes and the cardiovascular event or disease (such as coronary heart disease (CHD), myocardial infarction, heart failure, or stroke). In addition, the existence of additional microvascular problems, sex, age, BMI, blood pressure, glucose regulation and HbA1c levels, and smoking status are risk factors for CVD in people with diabetes [1].

5.1 Macrovascular Complications of Diabetes Mellitus

Diabetes is a significant risk factor for coronary heart disease, which raises the possibility of heart attacks. Insulin resistance, hyperglycemia, and other risk factors, such as dyslipidemia and hypertension, work together to cause atherosclerosis and coronary artery disease in diabetics. Diabetes raises the risk of stroke, both hemorrhagic and ischemic, due to cerebrovascular illness.

Cerebrovascular disease can occur more quickly when there is hyperglycemia, endothelial dysfunction, and other vascular abnormalities related to diabetes [10].

5.1.1 Cardiomyopathy and Arrhythmias

Peripheral artery disease (PAD) is a major risk factor for diabetes and can result in limb ischemia and amputation. Peripheral artery disease results from the interaction of diabetes-related atherosclerosis, neuropathy, and poor wound healing [11].

5.2 Periodontal Disorders

According to estimates, periodontal diseases rank as the sixth most frequent result of diabetes mellitus. There is established evidence linking diabetes to periodontal diseases in two ways: first, diabetes increases the risk and harshness of periodontal diseases; second, periodontal infections may exacerbate diabetes patients' inability to control their blood sugar levels [12].

Diabetes increases the risk of establishing periodontal disease for a number of reasons, such as altered collagen metabolism, compromised immunological function, and modifications to the microvascular structure [13].

Conversely, periodontal infections may make it more difficult for people with diabetes to regulate their blood sugar levels by resulting in chronic inflammation and resistance to insulin. It has been demonstrated that treating periodontal issues helps diabetic patients effectively control their blood sugar levels, emphasizing the necessity of incorporating oral health care within an all-encompassing diabetes treatment plan [14].

6. Role of Lifestyle in the Onset of Diabetes

Globally, over the past few years, there have been significant rises in both the frequency and prevalence of diabetes, particularly in newly developed and emerging nations. In fact, low- and middle-income countries currently account for 80% of all people with diabetes, and this percentage is still alarmingly rising. Lifestyle factors contributing to obesity, such as bad eating habits and a lack of physical activity, are the leading causes of the increase [15].

The contemporary sedentary lifestyle and the sharp rise in obesity worldwide are the primary causes of type 2 diabetes mellitus [16]. Concerns about obesity are also growing among fertile women. Being overweight, GDM and bad lifestyle choices are related [6].

6.1 Diet

The global obesity and type 2 diabetes epidemics are primarily caused by excessive calorie consumption, but diet quality also has its consequences. Regardless of BMI and other risk variables, carbohydrate and fat intake is a significant determinant in the development of diabetes [5]. More trans-fat and dietary glycemic load (GL) are specifically linked to an increased risk of diabetes while consuming more cereal fiber and polyunsaturated fat is linked to a lower risk [5]. Research also suggests that even after accounting for the impact of body weight, consuming more sugar-sweetened beverages (SSBs) raises the risk of type 2 diabetes [16].

Rapid social and economic development is joint in emerging countries, and changes in food patterns and lifestyle choices accompany this. These modifications encourage positive energy

balance and overnutrition. For example, traditional dietary practices are disappearing from Asia as people adjust to more mechanized and urban dining situations. Concurrently, constructed living spaces have grown more and more sedentary. These modifications raise the risk of type 2 diabetes by increasing fat accumulation in the lower torso around the abdominal area and body weight while lowering physical activity levels. In many developing countries, dietary shifts have been prompted by globalization and economic development. This change in diet usually entails consuming more animal fat and high-energy foods, consuming less fiber, and consuming fast food more frequently [17].

6.2 Physical Activity

Sedentary behaviors raise the risk of diabetes, while increased physical activity lowers that risk [4, 16, 18]. According to Hu [18], there was a 14% increase in the incidence of diabetes for every two hours spent viewing television during the day in the Nurses' Health Study (NHS). There was a 12% decrease in risk for every two-hour increment of standing or moving around at home daily. Walking briskly for one hour daily was linked to a 34% decrease in risk. These findings suggest that the association between exercise level and the risk of diabetes is not linear. Prolonged TV watching was linked to the highest risk among sedentary habits (TV, watching, sitting at work, and other sitting). The positive correlation between TV watching and the risk of obesity and diabetes can be explained by at least two different processes [17].

First of all, viewing TV usually replaces exercising. Hence, less energy is dissipated. Meanwhile, the greater likelihood of obesity and diabetes is not significantly reduced when recreational activities are taken into account. The consequences of TV watching remain unaffected by physical activity. The implementation of lifestyle modifications during pregnancy has promise in averting the onset of problems such as Gestational Diabetes Mellitus (GDM) [6]. According to García-Molina et al. [16], lifestyle changes can boost type 2 diabetes mellitus's glucose control significantly. This is especially true when the intervention involves diabetes education on self-management, both private and group sessions are combined, and/or last for a longer time, as well as when weight loss exceeds 5% of initial BMI. Improved type 2 diabetes mellitus management is possible with the help of these findings. Other cardiovascular disease risk factors may also be impacted, in addition to the glycaemic management of diabetes. Experts in medicine ought to persist in cautioning against gaining too much weight during pregnancy because it has been linked to large-for-gestational-age newborns, elective cesarean sections, and weight retention following delivery [6].

7. Role of Environment in the Management of Diabetes

Diabetes is a degenerative disease that modifies the body's metabolism of glucose (glucose). Individuals with diabetes are either unable to use insulin efficiently or do not create enough of this hormone, which controls blood sugar [19]. Although glucose is a vital energy source for body cells, individuals with diabetes either cannot use glucose well or do not make enough insulin. This causes the blood to contain excessive glucose levels, which over time may lead to various health issues [20].

Uncontrolled diabetes can lead to a host of grave health issues, including stroke and heart disease, as well as damage to the kidneys, eyes, and nerves. By closely monitoring and managing

their blood sugar levels, people with diabetes can reduce their risk of complications [21]. Numerous symptoms associated with diabetes, such as fatigue, thirst, and frequent urination, can make daily living more challenging and reduce overall quality of life. When diabetes is managed, people may see a decrease in the intensity of these symptoms and an improvement in their general health. Individuals with type 2 diabetes should focus mainly on managing their weight since being overweight may make it more challenging to maintain normal blood sugar levels [22]. Losing weight and avoiding weight gain are the two most crucial parts of diabetes management. Individuals with diabetes are more likely to experience other health issues, such as elevated blood pressure and cholesterol. Individuals who effectively control their diabetes reduce their risk of contracting these diseases. Diabetes can be managed partly by adopting healthy lifestyle choices, such as quitting smoking, eating a balanced diet, and getting frequent exercise. These choices might improve overall health and reduce the likelihood of developing new medical issues [23].

8. Environmental Factors that Affect Diabetes Management

8.1 Diet and Nutrition

Diabetes therapy necessitates close consideration of both nutritional intake and food selections. An appropriate diet may help control blood sugar and avoid complications related to diabetes [24]. Diabetes is a disorder in which the body either cannot make enough insulin or cannot use the insulin it does produce properly. Two main factors contributing to the growth in the incidence of diabetes are sedentary lifestyles and inappropriate dietary habits [25]. The current dietary guidelines for managing type 2 diabetes include elevated intake of low-glycemic index sources of carbohydrates, complex carbohydrates, fatty fish, and low-fat dairy products. People are advised to eat less foods rich in trans and saturated fatty acids [26]. Nutritional guidance should always be the first step in managing type 2 diabetes. It could help patients make decisions like meal planning that consider the kind, quantity, and timing of meals and control blood sugar levels. When type 2 diabetic patients get nutritional advice, their blood sugar levels and compliance with their recommended diet may improve [27]. In some circumstances, medicinal plants may be part of the therapy for diabetes. Numerous plants have been demonstrated to have the capacity to reduce blood sugar levels, which may help postpone the symptoms of diabetes [28].

8.2 Physical Activity and Exercise

Regular physical activity, including exercise, is crucial for managing diabetes. Exercisers with diabetes are more likely to have better glucose regulation, fewer cardiovascular risk factors, and better general health [29-31]. The American College of Sports Medicine has recommended that people with type 2 diabetes reduce their sitting time and exercise regularly [30]. The Association of British Clinical Diabetologists acknowledges the critical role that physical activity, including exercise, plays in preventing and treating diabetes [29]. Individuals diagnosed with type 2 diabetes are advised to engage in two to three resistance, flexibility, and/or balance training sessions per week in addition to 150 minutes of moderate-to-intense physical activity or 75 minutes of vigorous physical activity each week. Additionally, it is advised to divide prolonged sitting sessions into shorter ones [31]. Diabetes patients frequently struggle to exercise because they lack the energy and willpower to do so. Age, body mass index, sexual orientation, and hemoglobin A1c are all

associated with low levels of physical activity [32]. Furthermore, physical activity plays a major part in preventing type 2 diabetes [33, 34].

8.3 Air Pollution

Pollution is one example of an environmental element that may impact managing diabetes. There is a link between high air pollution levels and a higher risk of developing type 2 diabetes [35]. This work merged environmental data from air quality maps derived from satellite data gathered by remote sensing with a clinical-administrative dataset including around one thousand type-2 diabetes patients. The study found that in several of the regions it looked at, there is a relationship between seasonal variations in glycated hemoglobin levels and air pollution [35]. Research indicates that long-term exposure to air pollution is associated with adverse health effects, including a higher risk of respiratory illnesses, cardiovascular disease, and cancer [36]. Greater exposure to particulate matter with an aerodynamic diameter of less than 2.5 microns was linked to an increased risk of developing gestational diabetes mellitus (GDM), according to research by Zhang et al. [37]. The sources of nutrients in a person's diet may change due to exposure to air pollution, which might thus change the relationships with GDM [37].

8.4 Temperature and Weather

The weather and temperature might have an impact on diabetes therapy. One study's findings [37] indicate that temperature, holiday observance, and weekend scheduling significantly influence the population's typical glycemic metrics. The results of another study demonstrated a correlation between air pollution and the seasonal patterns of glycated hemoglobin in particular geographic areas [35]. The leading cause of the notable variations in blood pressure measurements from season to season is the environment's average temperature. If blood pressure-lowering medications are not adjusted for the seasons, this raises the risk of insufficient and overtreatment [38]. Extreme temperatures may affect the effectiveness and storage capacity of insulin, which may have implications for the management of diabetes [39]. Individuals with diabetes should take precautions during extreme weather, such as ensuring they don't become dehydrated and avoiding prolonged exposure to extremely high temperatures [39].

8.5 Stress

Stress may make it more difficult to adequately manage diabetes. Individuals with type 2 diabetes may discover that stress affects their capacity to control their blood glucose levels [40]. It has been found that cognitive-behavioral stress management can help pregnant women with gestational diabetes feel less stressed, which can improve the pregnancy's outcomes [41]. When Latinos with type 2 diabetes took part in a randomized controlled trial of a stress-management intervention delivered by community health professionals, improvements were observed in their psychological well-being, glycemic control, and cortisol levels [42]. Diabetes treatment is heavily influenced by hormones and how they are managed. The relatively new idea of emotional intelligence has the potential to provide an organizational framework for our knowledge of how emotions affect how well diabetes is managed [43]. Diabetes treatment will be improved by simulating the effects of acute psychological stress and physical exercise on glucose concentration

measurements. This will enable informed decisions regarding meal time, activity level, and insulin dose [44]. In African American adults with prediabetes and self-reported life stress, a mindfulness-based stress management program in conjunction with diabetes risk-reduction education is both feasible and effective in reducing stress-related physiology and improving engagement in risk-reducing lifestyle changes [45]. This was discovered to be the case for both the enhancement of involvement in risk-reducing lifestyle adjustments and the decrease in stress-related physiology.

9. Strategies for Managing Diabetes in Different Environments

9.1 Managing Diabetes in Urban Environments

Urban settings provide special possibilities and problems for managing diabetes. Cities affect people's capacity to properly manage type 2 diabetes as well as their chance of getting it [46]. Cities have a concentration of opportunities, people, and resources, which can improve health outcomes but also concentrate on dangers and health hazards, such as type 2 diabetes [46]. Cities are key for designing therapies because of their structure and content, including size, density, diversity, and complexity. These factors allow for studying the forces underlying type 2 diabetes [46]. Because diabetes has expensive long-term effects, it must be well managed in urban settings. Nevertheless, only a few diabetics receive the best possible care [46]. In order to address this, studies have demonstrated that including community health professionals in interventions has improved patient self-management practices and diabetes treatment [47]. Furthermore, diabetes self-management education and support (DSMES) can be critical in urban settings. It offers patients evidence-based instruction to help them learn the skills and information necessary to control their diabetes [48]. An interdisciplinary strategy that takes into account the special possibilities and difficulties that come with living in a city is essential for managing diabetes in urban settings. Urban regions can benefit from interventions like DSMES and community health professionals, which can enhance diabetes treatment and self-management [49].

9.2 The Therapeutic Management of Diabetes in Urban Areas

To stop or postpone the onset of diabetic complications, strict glycemic control must be achieved through a combination of dietary changes, oral antidiabetic drugs, and insulin therapy. To inform therapy modifications, blood glucose levels must be regularly monitored by self-monitoring or routine HbA1c testing [50, 51]. To lower the risk of macrovascular complications, including coronary heart disease and stroke, aggressive management of cardiovascular risk factors is essential. These risk factors include obesity, dyslipidemia, and hypertension. To control these risk factors, doctors may prescribe statins, ACE inhibitors, angiotensin II receptor blockers, and antithrombotic medicines [52, 53].

For early detection and prompt enforcement, routine screening for microvascular complications—such as diabetic retinopathy, nephropathy, and neuropathy—is crucial. Treatments for diabetic kidney disease and neuropathy may involve intravitreal injections, laser therapy, and medication. For complete diabetes management in urban settings, a multidisciplinary team approach combining endocrinologists, primary care physicians, ophthalmologists, nephrologists, and diabetes educators is essential. The different facets of diabetes, such as medication administration, lifestyle changes, and the detection and management of complications, can all be

addressed with the support of this team-based care [51]. Giving patients thorough diabetes education is crucial to enabling them to participate actively in their care. This education should cover managing the condition, changing lifestyles, and self-care. Patients may find it easier to deal with the difficulties of managing their diabetes in metropolitan environments if they have access to support services such as diabetes support groups and community-based initiatives [50].

9.3 Managing Diabetes in Rural Environments

The management of diabetes poses distinct obstacles in rural areas because of restricted access to healthcare, nutritious dietary alternatives, and transportation. The prevalence of diabetes is around 17% greater in rural regions than in urban ones [47]. Diabetes is more common in rural areas due to factors including more excellent obesity rates, less access to healthful meals, and fewer transportation alternatives. In addition, those who live in rural regions sometimes struggle to get the proper treatment because of factors including distance from clinics, limited financial resources, and cultural obstacles [54]. Customized, long-lasting, and reproducible interventions are required to address these issues. Numerous approaches have surfaced as potential solutions for enhancing diabetes care in remote regions, such as web-based initiatives, telemedicine initiatives, phone hotlines, and community health workers' assistance [55]. By removing obstacles to healthcare and health education in rural areas, these initiatives hope to improve diabetes treatment and self-management in the long run [48]. Targeted interventions are necessary in rural locations, considering the particular difficulties that these populations experience, such as restricted access to healthcare and wholesome food alternatives. In remote locations, diabetes care can be enhanced using customized approaches such as community health worker support and telemedicine initiatives.

9.4 Therapeutic Management of Diabetes in Rural Areas

Because of the restricted access to resources, healthcare facilities, and specialized care, this poses particular obstacles. To address these issues and enhance diabetes management in rural areas, several programs and interventions have been created. Community health workers (CHWs) in Indonesia are involved in this community-based intervention program, which includes education, follow-up care, and counseling for chronic illnesses such as diabetes. Significant improvements in risk variables like diabetes, hypertension, alcohol use, and high cholesterol have been demonstrated by the program. Patients with diabetes and other chronic diseases are also living longer because of regular visits to Posbindu-NCD [56].

An organized educational initiative in rural regions attempted to increase participants' understanding of managing hypoglycemia in diabetics. The majority of participants in the study had sufficient knowledge about controlling hypoglycemia following the intervention, demonstrating notable gains in their comprehension of this crucial component of diabetes care [57]. Patients with Type 2 diabetes in rural areas had much greater levels of spiritual well-being than those in urban areas, according to a study comparing spiritual well-being in these two settings. This implies that managing spiritual well-being can be crucial to managing diabetes, especially in rural areas where social support networks might be more robust [58]. To reach marginalized groups, the National Diabetes Prevention Program (DPP) has been developed for digital platforms.

Notwithstanding the difficulties, research on the Lark DPP, a digital DPP, revealed that individuals lost weight in a comparable way whether they lived in an urban or rural region [59]. This suggests that digital programs can be successful there. Innovative strategies that use digital technologies, organized education programs, and community resources are needed for the therapeutic management of diabetes in remote locations. These therapies, which address important risk factors and promote self-care habits and spiritual well-being, can significantly improve diabetes outcomes.

9.5 Gender Difference in Diabetes Mellitus

The prevalence, risk factors, and diabetes treatment vary significantly by gender. Even after controlling for BMI and other risk variables, women are more likely than males to develop type 2 diabetes. Nevertheless, despite the higher incidence in women, the occurrence of diabetes is often higher in men than in women in most nations [60].

Compared to men, obesity is a more significant risk factor for diabetes in women, and smoking increases the risk of diabetes in women. Furthermore, women are more likely than males to experience the detrimental effects of diabetes on health, including cardiovascular risk and death [1]. In addition, ovarian, endometrial, and postmenopausal breast malignancies are more common in diabetic women than in non-diabetic women [61]. Although diabetes care has become better for both sexes in recent years, women with diabetes still need to pay extra attention to obesity and smoking because these risk factors have not changed as much. Generally, gender-specific preventative and management approaches are critical to maximizing the treatment of diabetes [62].

10. Conclusion

The environment greatly influences the management of diabetes. People with diabetes may have worsening health effects if they are exposed to environmental risks such as air pollution and intense heat. Some ecological variables, including walkability, climate, pollution, dietary environment, and physical activity, can influence the risk of type 2 diabetes. Urban settings affect people's capacity to successfully manage type 2 diabetes as well as their chance of getting it. However, the lack of access to transportation, wholesome food alternatives, and healthcare makes living in rural areas more difficult. To address these issues, customized, long-lasting, and repeatable interventions—such as telemedicine initiatives, web-based initiatives, phone hotlines, and community health professionals' support—are required.

Author Contributions

OAO and DER contributed to the conception and design of the study. Material preparation, data collection, and analysis were performed by BAA, MI, TCM-A, TDO, DER. The draft was critically reviewed by BAA, MI, TCM-A, TDO, DER and OAO. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Competing Interests

The authors have declared that no competing interests exist.

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