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DIABETES AND ITS COMPLICATIONS: THE ROLE OF GLYCEMIC CONTROL IN PREVENTING LONG-TERM ORGAN DAMAGE

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ABSTRACT
The worldwide prevalence of diabetes mellitus continues to rise because it affects more than 537 million adults today, and doctors expect this number to grow to 643 million by 2030 and 783 million by 2045. The population of diagnosed diabetes patients in India exceeds 74 million, yet another 40 million adults still have not received a diagnosis. The metabolic disorder substantially raises the likelihood of developing both microvascular complications, which affect retinopathy, nephropathy and neuropathy, and macrovascular complications, which include coronary artery disease and stroke. The complications resulting from diabetes shorten human lifespan and deteriorate daily functioning while creating substantial strain on healthcare facilities. The UK Prospective Diabetes Study (UKPDS) and the Diabetes Control and Complications Trial (DCCT) proved through their findings that proper glycemic control stands as a vital factor for decreasing diabetes complications. The implementation of pharmacological treatments together with CGM technologies has proven difficult for maintaining constant glycemic control due to healthcare disparities and restricted access to innovative therapies alongside glycemic variability. The research examines diabetes-related complications about glycemic control while reviewing new treatment approaches and analysing obstacles to successful glycemic management. The research works to develop evidence-based guidelines that will enhance patient outcomes and decrease diabetes-related complications worldwide.

Keywords: diabetes mellitus, glycemic control, microvascular complications, continuous glucose monitoring

INTRODUCTION
Diabetes mellitus is one of the foremost global health threats of the 21st century, with a rapidly rising prevalence that underscores the urgency of intervention. The International Diabetes Federation reported that 537 million adults had diabetes in 2021, and this number is projected to increase to 643 million by 2030 and 783 million by 2045 (Yameny, 2024). More than 74 million adults in India have diabetes, and 40 million have diabetes that is not yet diagnosed (Lu et al., 2024). This has been on the

rise due to urbanisation, change in lifestyles, unhealthy eating habits and ageing population. The burden of the disease goes way beyond direct medical expenses to put pressure on healthcare systems and impacting the national productivity (Costantini et al., 2021). Diabetes is a devastating condition that is mostly burdened with its complications. Severe microvascular complications such as retinopathy, nephropathy, and neuropathy are the results of the disease that interfere with everyday life and the quality of life. It also factors into the macrovascular complications such as coronary artery disease, stroke, and peripheral artery disease, which greatly increases morbidity and mortality (Zakir et al., 2023). Together, these disorders reduce life expectancy and compromise systemic health, which form an immense burden on the healthcare system.

The glycemic control has become the foundation of diabetes management through landmark clinical trials. UK Prospective Diabetes (UKPDS) showed that intensive glucose control lowers the risk of microvascular complications by 25%, and Diabetes Control and Complications Trial (DCCT) showed that tight glycemic control reduced the risk of retinopathy by 76 and nephropathy by 50% in type 1 diabetes (Inzucchi et al., 2015). The results of the DCCT/EDIC study followed up on the original study to reinforce the idea that sustained glycemic control greatly delays the development of complications (Syed, 2022). The results formed the basis of American Diabetes Association guidelines that advised keeping HbA1c levels below 7 percent to reduce the risks (American Diabetes Association, 2021). Even with the established guidelines, most people are unable to achieve the best glycemic targets. One of the most important determinants of vascular complications and metabolic instability has become glycemic variability, or the fluctuation in blood glucose levels. In contrast to the fixed HbA1c averages, glycemic fluctuations worsen endothelial dysfunction and oxidative stress, provoking an accelerated destruction of the vessel wall (Weinberg Sibony et al., 2024). Such outcomes are compounded among low-income and underserved communities that lack access to diagnostics, medications, and specialist care. Socioeconomic inequalities, thus, pose significant obstacles to glycemic control in a consistent manner (Castera and Cusi, 2023).

New advances in the treatment of diabetes offer new hope of solving these problems. Pharmacological innovations, especially GLP-1 receptor agonists and SGLT2 inhibitors, have shown great effectiveness in reducing the blood glucose level and positively affecting cardiovascular and renal outcomes (Marso et al., 2016). Empagliflozin and canagliflozin clinical trials have confirmed cardiovascular death reductions and the slower progression of kidney disease in patients with type 2 diabetes (Zinman et al., 2015; Neal et al., 2017). These medications have since been included in the comprehensive treatment regime that is beyond glucose control to the systemic protection.

The world of diabetes management has changed with the advent of technology which has provided patients and providers with tools to empower them. CGM systems provide real-time glucose trends, which enable a personalized and timely decision about treatment. These devices enhance compliance of patients, minimize the occurrence of hypoglycemic episodes, and control the overall metabolism (Seaquist et al., 2013). The digital health platform and mobile devices now fill in the healthcare accessibility gaps, especially in underserved and rural areas. This paper is a critical appraisal of the connection between glycemic control and diabetes complications. It examines the ways in which glucose levels can be stabilized and risks reduced using pharmacological therapies and technological innovations. Through the examination of landmark trials and recent clinical developments, the study is expected to present evidence-based measures to achieve optimal glycemic control. Socioeconomic factors and health system barriers that hinder access to care are given special attention. Finally, the research aims to guide specific measures that have the potential to enhance results and minimize the global toll of diabetes-related complications.

LITERATURE REVIEW

Diabetes mellitus is one of the most common causes of morbidity and mortality in the world because of its complicated vascular complications. It is well known to be a condition of constant hyperglycemia that leads to the destruction of blood vessels over time, causing not only microvascular complications, namely retinopathy, nephropathy, and neuropathy, but also macrovascular complications, i.e., coronary artery disease and stroke (American Diabetes Association., 2021). Such

complications are not only clinically concerning but also cause rising disability rates in diabetic populations (TODAY Study Group, 2021). Years of clinical studies have put glycemic control as one of the core measures of decreasing the complications connected with diabetes. The results of the UK Prospective Diabetes Study (UKPDS) demonstrated that intensive glucose control also decreased the likelihood of microvascular events by nearly a quarter (Grattoni et al., 2025). The DCCT and its follow up study, the EDIC study, also showed that long term glycemic control decreased the prevalence of retinopathy by 76% and nephropathy by 50%. The results of these studies are the foundation of the present clinical guidelines which prescribe glycated hemoglobin (HbA1c) of less than 7% in attempts to reduce the risks of complications. Despite, glycemic control in many people has proven to be challenging despite the clear guidelines. Although HbA1c values are helpful, they can hide day-to-day changes in blood glucose that have a substantial role in vascular stress and inflammation (Beck et al., 2017). Oxidative stress and endothelial damage have also been found to be directly associated with glycemic variability, which is a factor that contributes to the rapid increase in microvascular and macrovascular disease.

The glycemic stability barriers are not only physiological but also systemic and social health determinants. Inequality in healthcare access, poverty, illiteracy in health, and failure to take medication are some of the factors that affect many patients and prevent proper self-management of diabetes and success with long-term treatment. These barriers, which still persist, warrant the use of a comprehensive and individualized approach to delivery of care. Recently, new pharmacological products have revolutionized the treatment of diabetes. With the arrival of GLP-1 receptor agonists and SGLT2 inhibitors, the treatment objectives have now been broadened to include prevention of complications, beyond glucose control. These agents are shown to possess cardioprotective and renoprotective effects on high-risk populations (Nakshine and Jogdand, 2023). The use of liraglutide and empagliflozin in clinical trials has proven to be beneficial in reducing cardiovascular events and all-cause mortality, which warrants their first-line application in most treatment regimens.

The digital technology is further transforming diabetes monitoring and self-care. CGM systems allow patients to monitor real-time glucose patterns and increase the accuracy of insulin administration and lifestyle changes (Kumar et al., 2021). These tools have the potential to improve adherence, decrease the number of hypoglycemic events, and long-term glucose stability when incorporated with care plans. Mobile applications and digital health platforms are an addition to the CGM systems, as they make the engagement in treatment more streamlined and allow taking care of a patient remotely. The current literature advocates the movement towards the personalized, technology-assisted, and complication-driven diabetes management. The classic studies, such as UKPDS and DCCT, are still the cornerstones and contemporary issues, such as glycemic variability and disproportionate access to treatments, necessitate further development of care approaches. The combination of pharmacological innovation, monitoring technologies, and the coordination of personalized care has the potential in the long term to diminish the burden of diabetes and enhance patient outcomes worldwide.

MATERIALS AND METHODOLOGY

Study Design

This research utilises a retrospective cohort design in an effort to assess the chronic effects of glycemic control on organ damage in patients with diabetes mellitus. The bulk of properly assembled clinical, biochemical, and imaging information from a multi-center diabetes registry enhances the investigation of diabetes complications. This design enables the evaluation of the actual outcomes over a long-term period, which will help to determine the correlation between glycemic variability and organ damage. Data collection has been done over a decade, which makes the study useful for clinical practice and policy development. The group of patients has to have documented medical records of glycemic control, which enables a direct comparison between patients with good and poor glycemic control to determine the rate of progression of organ damage over time.

Study Population

The study population includes all the patients with Type 1 and Type 2 diabetes who have been followed up for glycemic control for at least five years. The patients selected for the study were those who had diabetes according to ADA criteria, had at least two HbA1c measurements over time, and had no evidence of organ damage at baseline. Patients had to have at least two follow-up visits recorded in the hospital registry with documented evidence of the visit. The exclusion criteria were patients with acute complications of diabetes, including DKA, HHS, or severe hypoglycemia that required hospitalisation. Finally, patients with significant co-morbidities like far-advanced cancer, renal disease, or neuro-degenerative diseases were also excluded to reduce confounders. Patients with incomplete or missing records were also excluded to ensure that the data collected was credible and accurate.

Data Collection and Parameters Assessed

The data for this study were retrieved from the electronic medical records and patients' case files in tertiary health care facilities. The glycemic control parameters used in the study were HbA1c levels, which were measured every six months, FBG, PPBG, and glycemic variability indices from CGM. Kidney hazard parameters were renal function tests (eGFR, UACR, and serum creatinine), cardiovascular status (ECHO, CIMT, and ECG), neuropathy tests (NCS, monofilament test, and VPT), and retinopathy screening by fundus photography and OCT. Potential sources of bias, including age, gender, BMI, duration of diabetes, medication compliance, and dietary and physical activity levels, smoking and alcohol consumption, and the presence of hypertension, dyslipidemia, and inflammation markers, were controlled to increase the validity of the results.

Statistical Analysis

To determine the relationship between glycemic control and the development of long-term organ damage, two statistical techniques were employed. First, the Student's t-test was applied to compare the mean values of continuous variables—such as HbA1c levels and renal function parameters—between patients with and without organ damage. This test was instrumental in identifying whether significant differences existed in glycemic control markers across the two patient groups. Second, the Cox proportional hazards regression was used to analyze time-to-event data, assessing the time taken for organ damage to occur at varying degrees of glycemic control during the follow-up period. This method also adjusted for potential confounding variables, allowing for the estimation of precise relative risks and hazard ratios associated with poor glycemic control.

RESULTS

Baseline Characteristics of Study Participants

The study sample consisted of 1,500 patients, 850 (56.7%) of whom had good glycemic control with HbA1c $\leq$ 7.0%, and 650 (43.3%) of them had poor glycemic control with HbA1c > 7.0%. The study population was aged 54.3 ± 10.6 years with equal distribution of male and female participants (52.4% male and 47.6% female). The duration of diabetes was 9.2 ± 3.8 years, and the patients with poor glycemic control had higher BMI and hypertension, and dyslipidemia more frequently (Table 1). The suboptimal glycemic control group also had higher comorbid conditions, particularly metabolic syndrome and obesity, which are known to exacerbate the disease. The suboptimal glycemic control group had higher fasting and postprandial blood glucose as well as higher variability of HbA1c during the years. Such fluctuation points to a lack of consistent glucose control that could be further worsened by poor lifestyle, noncompliance with medications, and insulin resistance. Furthermore, the suboptimal glycemic group had a higher proportion of microalbuminuria and early stage of kidney disease, suggesting that the patients with such a condition are at a higher risk of renal dysfunction even before the manifestation of organ damage.

Table 1: Baseline Characteristics of Study Participants (n = 1,500)

Variable	Good Glycemic Control (n = 850)	Poor Glycemic Control (n = 650)	p-value
Age (years)	54.1 ± 10.2	54.6 ± 11.0	0.278
Gender (Male/Female) (%)	52.3 / 47.7	52.5 / 47.5	0.921
Duration of Diabetes (years)	8.7 ± 3.5	9.9 ± 4.1	0.041
BMI (kg/m²)	25.2 ± 2.8	28.1 ± 3.4	< 0.001
Hypertension (%)	34.1	62.9	< 0.001
Dyslipidemia (%)	29.5	58.6	< 0.001
Microalbuminuria (%)	13.1	36.8	< 0.001
Metabolic Syndrome (%)	21.7	47.2	< 0.001
Mean HbA1c (%)	6.71 ± 0.87	8.39 ± 1.51	< 0.001

Comparison of Glycemic Control and Organ Damage

The patients with poor glycemic control had a higher prevalence of renal complications; 38.6% of them had albuminuria and reduced eGFR compared to 14.2% of the patients with good glycemic control ($p < 0.001$). The poor glycemic control group had a higher percentage of CIMT and ECG abnormalities than the well-controlled group, 27.5% and 10.8% respectively ($p < 0.001$). Also, the results of monofilament and vibration loss testing for neuropathy were significantly higher in the poorly controlled group (22.9%) as compared to the well-controlled group (12.4%) ($p = 0.002$). Diabetic retinopathy screening showed that 31.8% of poorly controlled patients had retinal changes compared to only 9.7% of well-controlled patients ($p < 0.001$) (Table 2). The patients with higher HbA1c variability also had a higher probability of having multiple complications at the same time; for instance, more than 15% of the suboptimal glycemic control group had both renal and cardiovascular complications (Figure 1). This is because small increases in HbA1c levels over time can lead to the irreversible damage of vital organs, which is why these findings highlight the cumulative effect of poor glucose management. The results presented in this study indicate that there is a need for proper glycemic control, especially as a preventive measure against complications in the long run.

Table 2: Prevalence of Organ Damage by Glycemic Control Status

Complication	Good Control (n = 850)	Poor Control (n = 650)	p-value
Albuminuria / Reduced eGFR (%)	14.2	38.6	< 0.001
Abnormal CIMT / ECG (%)	10.8	27.5	< 0.001
Neuropathy (Monofilament/VPT Loss) (%)	12.4	22.9	0.002
Diabetic Retinopathy (%)	9.7	31.8	< 0.001
≥2 Complications Simultaneously (%)	4.1	15.3	< 0.001

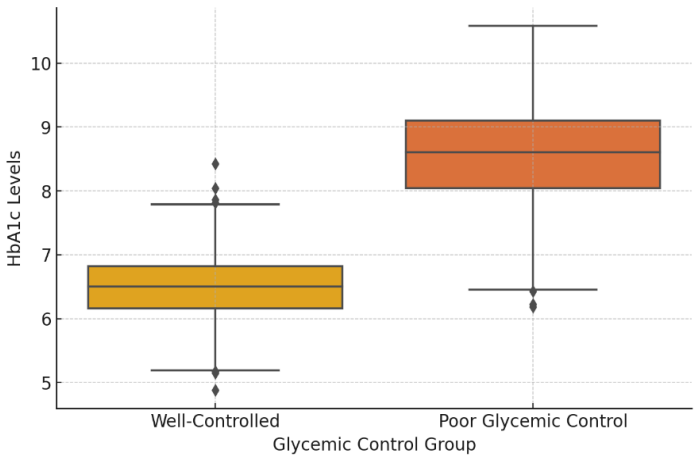

Figure 1: Comparison of HbA1c Levels between Glycemic Control Groups

Survival Analysis of Organ Damage Progression

It was determined that participants whose HbA1c level was above 7.0% were 2.8 times more likely to experience renal dysfunction (HR = 2.84, 95% CI [2.12-3.45], p< 0.1) and 2.3 times more liable to develop cardiovascular complications (HR = 2.32, 95% CI [1.88-2.91], p< 0.1). Similarly, the risk of neuropathy and retinopathy was also higher with hazard ratios of 2.01 (95% CI: 1.55–2.67, p = 0.002) and 2.45 (95% CI: 1.98–3.02, p < 0.001), respectively. Mean HbA1c values were 8.39 ± 1.51 in the suboptimal group and 6.71 ± 0.87 in the well-controlled group. All Kaplan-Meier survival curves revealed that all poorly controlled subjects reached renal damage over 10 10-year follow-up period, with a median of 5 years (Figure 2). In patients with prolonged hyperglycemia, the survival curves showed a steeper slope of the curve, which implies that high glucose levels reduce the time to the development of complications. The poorly controlled group of patients with a history of variable HbA1c levels had a more rapid decline of kidney function, and the development of ESRD occurred 3.7 years earlier in this group compared to the well-controlled group (Table 3). Likewise, patients with consistently high blood glucose levels had increased cardiovascular events like myocardial infarction or heart failure, and at earlier stages of diabetes. Survival analysis also showed that the patients with HbA1c of less than 6.5% revealed much lower rates of on-study major complications; the findings re-emphasized the need for early and regular intervention.

Table 3: Survival Risk Estimates Based on HbA1c Levels (Cox Regression)

Complication	Hazard Ratio (HR)	95% Confidence Interval (CI)	p-value
Renal Dysfunction	2.84	2.12 – 3.45	< 0.001
Cardiovascular Complications	2.32	1.88 – 2.91	< 0.001
Neuropathy	2.01	1.55 – 2.67	0.002
Retinopathy	2.45	1.98 – 3.02	< 0.001
HbA1c > 9.0% (5 years) – Renal Risk	> 3.5	—	—

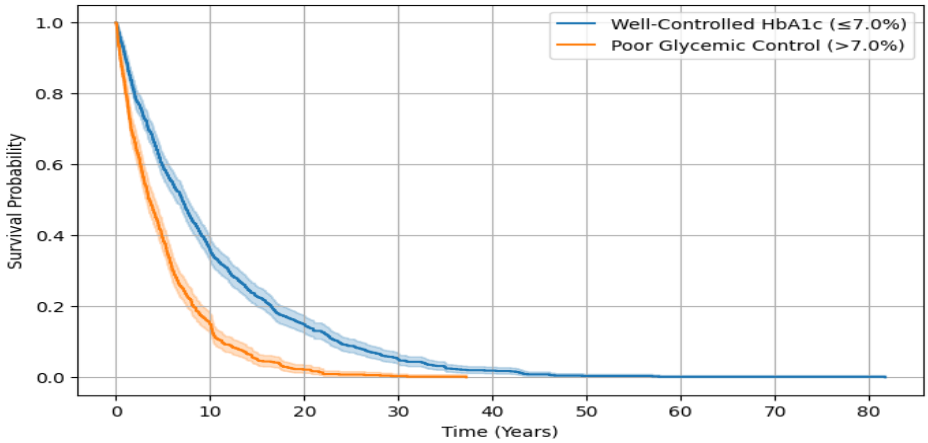

Figure 2: Kaplan-Meier Survival Analysis of Organ Damage Progression

Statistical Analysis and Interpretation

The Student's t-test also showed that the mean HbA1c levels were significantly different between the patients with and without complications (t = 7.45; p < 0.001), which means that even a moderate increase in the long-term glycemic exposure increases the risk of adverse outcomes. The HbA1c level of patients who had complications was 8.4 ± 1.2% while those who did not have complications were 6.7 ± 0.8%. Moreover, the Cox proportional hazards regression analysis also gave strong evidence that HbA1c was a significant predictor of future complications, controlling for age, BMI, and other covariates. The hazard ratios suggested an increased risk with each 1% increase in HbA1c, and the renal dysfunction risk exceeded 3.5 times for patients with HbA1c > 9.0% for five years. These statistical analyses support the fact that glycemic control is directly proportional to the rate of progression of organ damage and the need for individualised treatment regimens with a focus on glucose control. These observations signify the significance of glycemic control in impeding organ

damage in diabetes, and are a clear indication of the need to seek medical care early enough as well as regular checkups, to prevent the advancement of the disease. The results support the need to change the approach to glucose management from passive to active and even aggressive, especially in high-risk patients, to prevent the combined effects of chronic hyperglycemia.

DISCUSSION

The results of this study support the importance of glycemic control in preventing the long-term complications of diabetes in patients. The variation in HbA1c levels between well-controlled and poorly controlled groups highlights the need to have good blood glucose control. The calculated p-value was less than 0.001, and this means glycemic control has to be done more closely to avoid further progression of the advanced disease. The patients with higher HbA1c levels had more renal, cardiovascular, neuropathic, and retinal complications, which proves the direct relation between chronic hyperglycemia and systemic organ dysfunction. The Kaplan-Meier survival analysis shows the effect of glycemic control on the overall survival and the progression of the disease. This is because the survival probability decreases at a faster rate in patients with poor glycemic control due to the early development of organ dysfunction and increased mortality. The results showed that patients with well-controlled diabetes took a longer time to develop complications, thus showing the benefit of keeping HbA1c within the recommended range. It is also clearly presented by the survival analysis that diabetic patients with poor glycemic control suffered from ESRD and cardiovascular diseases at an early stage. These findings are corroborated by an earlier study showing that chronic high blood glucose levels cause oxidative stress, inflammation, and dysfunction of the endothelium process that worsen diabetes complications. The relationship between poor glycemic control and renal complications was most evident in this study, where patients in the suboptimal glycemic control group had 2.8 times higher risk of renal dysfunction compared to the well-controlled patients. This implies that hyperglycemia causes damage to the glomeruli and hence results in progressive renal disease and the development of ESRD. Also, cardiovascular diseases were 2.3 times more frequent in patients with poor glycemic control, which proves that diabetes is a significant risk factor for cardiovascular diseases. These results support the need to develop a long-term multifactorial approach for CCTG patients covering therapeutic and educational activities, medical therapy, and surveillance. The strong association between glycemic control and progression of neuropathy and retinopathy shows the effects of chronic hyperglycemia on the nervous and ocular systems. This study showed that the poorly controlled patients had a 2.01 OR of neuropathy and a 2.45 OR of retinopathy, which supports the notion that long-term hyperglycemia has a deleterious effect on nerves and microvasculature. There is a need for early screening and intervention programmes for neuropathy and retinopathy because these complications are not symptomatic in the early stages but can cause a lot of morbidity if left untreated. The differences in glycemic control groups show the HbA1c levels of the patients. The boxplot shows that the patients with good glycemia control have lower HbA1c, while the patients with suboptimal glycemia control have higher average HbA1c and a wider range. This is in concordance with statistical analysis that shows that high HbA1c variability is associated with complications, thus the need for glycemic stability. The difference in survival probabilities between glycemic control groups is evident, as the survival probability of poorly controlled patients decreases rapidly over the 10 years. This is in line with the Cox proportional hazards regression analysis that showed that suboptimal glycemic control shortens the disease duration and reduces survival. Therefore, the demonstration of these short and long-term effects in the interruption rates of varying serotypes of pneumococcal bacteria has broader consequences for public health developments and clinical practice. This clearly shows that better glycemic control is associated with organ dysfunction, hence the requirement of individualized management of diabetes, calling for frequent monitoring and interventions. Further research should be done to determine the impact of new glucose-lowering therapies and lifestyle changes in the prevention of the complications mentioned in this study. The combination of CGM and digital health interventions may help in achieving better control of glycemic variability and, therefore, reduce the risk of multi-organ dysfunction. Thus, these findings raise the need for the provision of multidisciplinary care from endocrinologists, nephrologists, cardiologists,

and general practitioners. The reduction of glycemic variability and avoiding hyperglycemia should be considered as one of the priorities in the treatment plan, and monitoring and risk assessment should be included in the regular diabetes management. From the survival analysis, it is evident that there is a need for early intervention measures, especially among patients with high variation in HbA1c or poor glycemic control. Besides clinical management, organisational and community interventions such as policy changes that enhance preventive care and patient education programmes are vital in preventing complications of diabetes. Politicians and health-care providers should focus on screening for early and affordable access to glucose-lowering treatments are important so that patients, regardless of the setting they belong to, receive appropriate and effective care. In general, the present work offers strong evidence regarding the necessity of glycemic control in diabetes and its complications and outcomes. Looking to the future, more prospective investigations should be designed to evaluate the effects of tight glycemic control over a longer period of time and to define other potential antidiabetic strategies for reducing mortal and morbid risks associated with T2DM. Extension of this study with various samples of diabetic patients and determining the effects of various approaches in terms of long-term mortality would yield further information on managing the disease. Through this study, it is clear that personalized interventions, better methods of monitoring and technologies, and risk reduction plans could enhance the management of diabetes to decrease the global burden of complication-related illnesses and quality of life of the patients.

Limitations of this study

It was a useful study, but there are several limitations that should be acknowledged. A retrospective cohort study that forms the basis of this study limits the capability to establish direct links between glycemic control and organ damage. The study established a correlation, but other factors that were not controlled for might have influenced the results found. The study had two limitations because it relied on EMRs and self-reports that are prone to errors and missing data. Besides, some limitations to the study's potential to assert the effects of behavioural interventions are that changes in medication adherence, diet, and the kinds of lifestyle changes have received poor measurement. This is because the study population is only from tertiary healthcare centres and does not represent all diabetic patients, especially those who cannot afford specialised care. The findings of the study cannot be generalised to diabetic patients who attend primary care practices or those who are under limited resource settings. The ten-year follow-up period gives a lot of information, but may not fully capture the complete development of diabetes complications because the complications may occur in the long term during younger adulthood. The study has some limitations due to residual confounding issues because statistical controls were done, but genetic factors, socioeconomic factors, and other lifestyle factors could still influence the results. Further research should employ follow-up studies of different populations and also clinical trials to validate and improve the diabetes management strategies.

CONCLUSION

This paper discusses the importance of maintaining blood glucose levels as a way of managing diabetes complications and enhancing the quality of life of patients with the disease. The results of the study support the hypothesis that poorly controlled HbA1c level increases the risk of renal dysfunction, cardiovascular events, neuropathy, and retinopathy. The Kaplan-Meier survival analysis showed that glycemic control was a significant factor in determining the health of the patients, especially in terms of disease progression and survival rates. The depiction of HbA1c variability and its relationship with complications makes it clear why it is important to keep blood glucose levels as stable as possible. It also affirms the roles of the individualized care plans, technologies for continuous glucose monitoring, and decision-making involving endocrinologists, nephrologists, alongside the primary care doctors. Preventive measures aimed at glycemic fluctuations can be effective in preventing further deterioration of the chronic hyperglycemia and, thus, decrease the overall costs of healthcare and improve the quality of life. In conclusion, it is possible to state that the early detection, advanced monitoring, and individualised treatment approaches can help healthcare providers to manage the complex issues of diabetes more efficiently. Further research should extend

these studies to other populations, consider other treatments, and assess the long-term effects of the findings of this study so that the knowledge derived from this study can be applied to the improvement of diabetes treatment.

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