Review Article

Continuous Glucose Monitoring with Real-Time Readings

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Abstract

With 74.2 million people affected, diabetes represents a major burden on India's health-care system and economy. Effective diabetes management is based on diet, lifestyle, pharmacotherapy, and glucose monitoring that are to be individualized for every patient. However, glucose monitoring rates in India are abysmal. The available monitoring techniques have limitations with respect to mostly being single point-in-time readings that may not be entirely reflective of the state of diabetes control. With advancements in technology, the new monitoring tool – continuous glucose monitoring (CGM) – provides visibility into the glycemic profile 24 × 7 with user-friendly reports that provide information much beyond the glycated hemoglobin (HbA1c) and self-monitoring of blood glucose. This innovative tool also detects the time spent in range by the individual with diabetes. This is the new metric endorsed by all reputed medical organizations for diabetes management with multiple benefits ranging from helping slow down the progression to diabetes-related complications to enabling improvement in overall glycemic control. CGM can be classified into personal and professional types based on its usage. Certain types of CGM can also provide real-time (RT) readings either automatically or on-demand. This review article explores the CGM technologies with RT readings in the context of diabetes care in India. These new technologies have the potential to change the way diabetes is managed today including making smart decisions such as the right choice of diet, apt lifestyle modification, and adequate titration of pharmacotherapy (including insulin) while monitoring glucose levels continuously anytime anywhere without a prick.

Keywords: Continuous glucose monitoring, glucose monitoring, glucose readings, glycemic profile, glycemic variability, interstitial fluid, mean absolute relative difference, real-time readings, self-monitoring of blood glucose, technology, time in range

Introduction

Noncommunicable diseases like diabetes have overtaken infectious diseases as the most common cause of death and now cause over 60% of all deaths in India.[1] They also pose a major economic burden as they are major causes of morbidity and mortality, and consume considerable health-care resources.[1] India currently holds the second position globally in terms of the number of people with diabetes, and an estimated one out of every six people in India have diabetes.[2] According to the Tenth Edition of the International Diabetes Federation Atlas 2021, there are 74.2 million people living with diabetes in India, and this number will increase to 124.9 million by 2045, by which time 783 million people will have diabetes worldwide.[3,4] What is more concerning is that there are 240 million people worldwide living undiagnosed with diabetes.

In India, like hypertension, diabetes also follows the "rule of halves" [Figure 1]. Thus, only about half of the diabetes cases are diagnosed. Within the pie of diagnosed diabetes, only around 50% take treatment, and of the latter, <50% are adequately controlled. This means that only about 12.5% of all people with diabetes have their diabetes under control. This lack of control is attributed to lack of awareness, insufficient monitoring, poor compliance, glycemic variability (GV), and often therapeutic inertia. Apart from the acute complications of diabetes such as diabetic ketoacidosis, hyperglycemic nonketotic coma, and hypoglycemia, it is the chronic

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complications due to damage to the blood vessels such as retinopathy, nephropathy, neuropathy, and cardiovascular diseases that contribute to morbidity, hospitalization, and mortality due to this metabolic disorder.[6] Diabetes alone drains around 5%–25% of average Indian household earnings. It is worth remembering that in India, over 70% of the medical expenses are paid out of pocket.[7]

The magnitude of the problem in the Indian context can be judged from the alarming figures that during 2004, diabetes has been directly responsible for 109,000 deaths, 1157 years of life lost, and 2263 disability-adjusted life years. This shows that lack of control of diabetes is linked to poor outcomes for patients.[8] Besides, our study evaluating the global burden of diabetes shows the alarming rise in diabetes cases between 1990 and 2016 [Figure 2].

As India is a geographically and culturally diverse country, diabetes is very heterogeneous across different states. The differences in the prevalence of diabetes between states might be explained by factors such as differences in socioeconomic status, physical activity, dietary patterns, obesity prevalence, and possibly genetic variation. In the Indian Council of Medical Research-India Diabetes study, we have presented the state-wise prevalence of diabetes and prediabetes in 15 states across the country [Figure 3]. The results have indicated a higher prevalence of diabetes among the lower socioeconomic groups within the urban areas of the more economically developed states.

Importance of Glucose Monitoring

If left untreated, diabetes has a natural progression to end-stage complications. Thus, maintaining good glycemic control is critical in the management of diabetes, especially in the early stage of the disorder, as this leads to what is known as a "good glycemic legacy." Good control is associated with a reduction in both macro-and microvascular complications of diabetes. Diabetes control is assessed by several monitoring techniques, i.e., self-monitoring of blood glucose (SMBG) and laboratory tests including hemoglobin A1c (HbA1c) and fasting and postprandial blood glucose levels. Unfortunately, monitoring is not given its due importance within the diabetes management domain.[13] SMBG has been historically used since the days of the Diabetes Control and Complications Trial and the United Kingdom Prospective Diabetes Study as a marker that denotes the level of glycemic control.[14,15] However, its adoption remains suboptimal, particularly in India. This is due to both patient and health-care practitioner (HCP)-related factors. Apart from the hurdle of painful skin pricks, SMBG also has the limitation that it is a single point-in-time reading with restricted insights, and this limitation has been described in various articles.[16]

Glycated hemoglobin (HbA1c), the gold standard in diabetes management, denotes the average level of blood glucose over a 2–3-month period. While it provides an excellent index of long-term control, it does not provide any insights into the daily

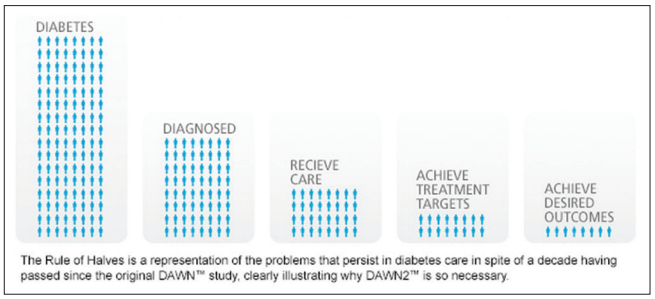

Figure 1: Rule of Halves framework[5]

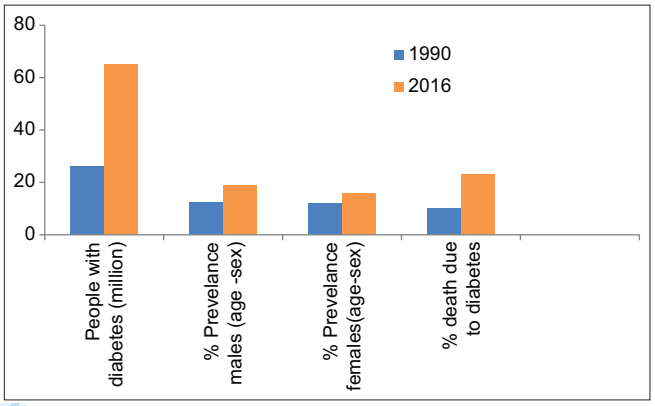

Figure 2: Estimate of diabetes status in India from 1990 to 2016[9,10]

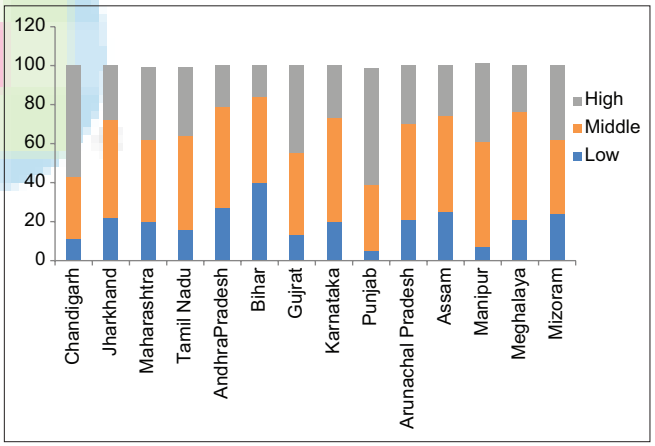

Figure 3: State-wise prevalence of diabetes and prediabetes as per socioeconomic status in 15 states across the country[11,12]

glucose fluctuations. Moreover, studies have demonstrated that two patients with the same HbA1c can have different degrees of fluctuating glucose.[17,18]

Laboratory tests such as fasting plasma glucose (FPG) and postprandial plasma glucose (PPG) are frequently ordered by the treating HCPs to understand the glucose behavior of patients with diabetes and make changes in their prescriptions. However, these tests only reflect the glucose status on that given day. In a country like India, where high carbohydrate meals are traditionally consumed three times a day, the information provided by FPG and PPG (that too done sporadically) does not match the true state of diabetes control.

In this context, glucose monitoring took a quantum leap with the introduction of continuous glucose monitoring (CGM), which measures glucose levels within the interstitial fluid, continuously, 24 × 7, for varying durations of time, even up to 2 weeks. This is made possible by the use of a portable device which, once applied, collects glucose readings every 1–5 min continuously day and night without any fingerpricks. This technology thus overcomes the limitations of existing monitoring techniques outlined above.[19]

Continuous Glucose Monitoring Technology and its Role in Diabetes Management

In 1999, a new era in diabetes care began when the first-ever CGM system was approved for the treatment of diabetes. The development of this new technology allowed patients to monitor their blood glucose by inserting a device subcutaneously. The CGM system measures a patient's glucose levels in their interstitial fluid over the entire day. Earlier versions of CGM have several challenges including lag time as well as accuracy. However, significant advancements have been made in terms of user-friendliness and much higher accuracy levels have been achieved.[20]

CGM, in contrast to earlier mentioned techniques, provides not only one snapshot of glucose readings but also an insight into the glycemic profiles day and night without disrupting the patient's sleep or lifestyle. It is like comparing a video with a still photograph. CGM is especially useful in patients with hypoglycemia unawareness. It even helps to determine the effect of high glycemic index foods and exercise on the glucose levels of patients with diabetes. The continuous data allow us to look at GV – the first-ever tool that helps visualize/detect and also quantify GV without any mathematical calculations. With the various detailed reports it offers, this technology also serves as an educational tool for patients to understand their diabetes better and take ownership towards managing their lifestyle, and this improves their glucose control.

CGM is also of great help in identifying or unmasking underlying issues in glucose control to make changes and helps in formulating treatment prescriptions, and subsequently assessing the impact of the treatment given.[21,22]

CGMs can be classified into professional and personal CGMs. See Table 1 for differences enumerated between these two CGM types. As the name suggests, professional CGM is meant for use by the treating HCPs and it provides a set of reports that can be downloaded for discussion between the HCP and the patient. On the other hand, the personal version is a personal device that is intended for the patients' use to track their glucose levels. In India, we have both the professional and personal versions of CGM available for the HCPs and for patients to assess their diabetes control.[23]

Thanks to rapid developments in technology, today, CGM devices are connected to the cloud and can communicate wirelessly with both the HCP as well as the person with diabetes upon a single scan of the CGM sensor. These advancements are indeed revolutionary and have brought about a paradigm shift within the diabetes monitoring space and have the potential to improve clinical outcomes of diabetes.[20,24]

Real-Time Continuous Glucose Monitoring

The real-time CGM (RT-CGM) is a compact system, where there is continuous monitoring of the glucose levels more or less in RT.[20] The system is hassle-free, avoids finger pricks, and provides 288 glucose readings in a single day. There is a 20-min delay of the glucose concentrations in the interstitial fluid compared to the blood glucose readings. RT-CGM is highly beneficial and preferable for the detection of nocturnal or unidentified hypoglycemia and GV. It provides RT readings ranging from up to 5–6 days to up to 10–14 days. The usage of RT-CGM has been shown to reduce the incidence of hyperglycemia. The mean absolute relative difference (a measure of the accuracy of the CGM systems) of the latest device is extremely low, showing their precision and accuracy.[25,26]

This technology is rapidly gaining popularity, just like the electrocardiogram was adopted decades ago. CGM also provides an insight into the time-in-range (TIR) which is the most recent metric for glucose control endorsed by various medical organizations and societies. It is now universally agreed that a TIR of at least 70% (i.e., blood glucose is under control for 70% of the time in a day – which represents good glucose control for 16.8 h out of the 24 h in a day) would help to prevent the complications of diabetes. TIR is directly related to HbA1c in both Type 1 diabetes (T1DM) and Type 2 diabetes (T2DM). Every 10% increase in TIR brings ~0.5% reduction in HbA1c in T2DM and ~0.8% reduction in HbA1c in T1DM and T2DM. In various published studies, the use of TIR is effective at improving diabetes outcomes through the benefits offered [Figure 4].[27-29]

Limitations of continuous glucose monitoring

Lag time

As CGM sensors detect the glucose level in interstitial fluid rather than in the blood, there are concerns about the lag time resulting in differential readings between the two mediums.[30] However, this slight delay does not detract from the usefulness of the device. It must be remembered that it is currently not possible to stick a sensor into a blood vessel periodically to

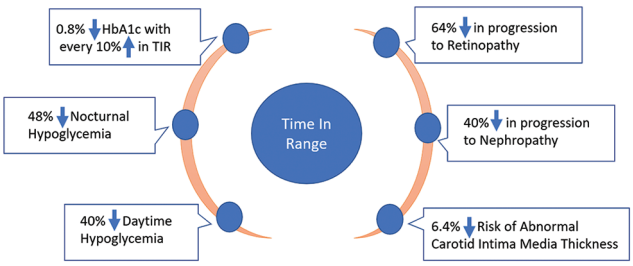

Figure 4: Benefits of time in range[27-29]

Table 1: Types of continuous glucose monitoring and differences

Parameters	Types of CGM	
	Professional CGM	Personal CGM
Owned by	Health-care professionals	Patients him/herself or caregivers
Real-time readings	No	Yes, in the case of a real-time CGM
Analysis	CGM data analyzed by healthcare professional	Patients can take decisions according to hypo/hyperglycemia
AGP graph	Allows detection of trends and patterns of hypo/hyperglycemia, glucose variability, and hidden glycemic problems	Patients can use a daily graph summary to see when and where their glucose was in and out of the target range
Advantages	It gives a clear picture of the most probable behavior of blood glucose and outliers	Increases TIR
	Allows detection of unknown hypoglycemia	Provides a detailed view of day-to-day glucose reading that helps patients
	Helps HCP and patients to discuss intervention areas through diet and lifestyle	Shows daily variability of glucose levels
		Reduction in HbA1c, hospitalization, and work absenteeism

CGM: Continuous glucose monitoring, AGP: Ambulatory glucose profile, TIR: Time-in-range, HCP: Health-care practitioner, HbA1c: Hemoglobin A1c

get blood glucose readings as it could lead to serious clot formation.

Calibration

Earlier CGM systems required daily calibration with finger-stick glucose measurements to get a more accurate reading by the sensor.[31] However, the recent CGM devices introduced by Abbott overcome this issue as they are factory calibrated.

Adoption

In India, the cost of using CGM regularly for prolonged periods of time could be a barrier for many patients. However, intermittent use of CGM can help in reducing the cost.[32]

Evidence Supporting Continuous Glucose Monitoring with Real-Time Readings in Diabetes Management

Daily monitoring of diabetes is mandatory to keep a check on how particular food habits, physical exercise, and medications affect the glucose level in different individuals. The use of CGM with RT readings makes this easier, safe, and patient-friendly without painful finger pricks.[33]

In our study published on experience with the professional version flash glucose monitoring system, benefits ranging from significant reductions in glycemic parameters such as HbA1c/FPG/PPG to optimizing insulin doses in patients with T1DM and T2DM were reported.[34,35] Another Indian study in T2DM patients showed that the use of CGM led to significant HbA1c reduction, insights for enabling changes in the treatment protocol, and better patient compliance.[35,36]

Recent evidence using RT-CGM shows that patients using this device spent less time in hyperglycemic and hypoglycemic episodes; conversely, they increased the time spent within the set target range of 70-180 mg/dL, i.e., the TIR when compared to the control group. Using the CGM system led to improvement in glycemic control with less glucose variability and hypoglycemia.[37,38]

Conclusions

Diabetes is a chronic disorder that contributes to morbidity and mortality. The overall control of diabetes in India remains poor, with only one third of people with diabetes achieving the HbA1c target of <7%. Thus, the burden due to macro-and microvascular complications remains high. Therefore, there is an urgent need for maintaining good glycemic control in all individuals with diabetes. This can be achieved with the help of new technologies like CGM with RT readings that can help improve metabolic control, reduce hypoglycemic episodes, and improve the quality of life. In the long term, CGM would help to reduce chronic diabetes complications and perhaps also morbidity and mortality, thereby reducing health-care costs. All these, in turn, would help improve the quality of life of patients with diabetes in India. More studies are needed to document all these in Indian patients with diabetes.

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Conflicts of interest

There are no conflicts of interest.

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