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Review Article

Artificial Intelligence Aided Continuous Glucose Monitoring and its Effectiveness in the Management of Type 2 Diabetes; A Narrative Review

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Abstract

This literature review offers a thorough summary of current research on continuous glucose monitoring (CGM) for the treatment of diabetes. Continuous glucose monitoring is a non-invasive technique proven efficient in enhancing diabetes management by reducing HbA1C and achieving better sugar control. Patients who use CGM for managing their diabetes have also experienced decreased fear of hypoglycemia and improved diabetes self-management skills, increasing their confidence to control their blood sugars efficiently. Although data management is challenging, CGM systems offer helpful insights into glucose levels for the management of diabetes. The review covers various CGM-related topics, including accuracy, efficacy, patient outcomes, technological advancements, patient challenges, limitations, and future research recommendations referring to the literature published in the past on the topic. The review also discusses optical signalling, biosensors, and other technologies used in glucose-sensing technology for continuous monitoring.

Keywords: Continuous glucose monitoring; Diabetes; Glycemic control; Blood sugar tools; Artificial intelligence; Glucose level; Type 1 diabetes; Type 2 diabetes.

Introduction

The term "diabetes mellitus" describes a collection of illnesses brought on by abnormalities in the body's glucoregulatory system resulting in Hyperglycemia [1]. Chronic hyperglycemia, due to uncontrolled diabetes is linked to long-term complications such as organ failure and tissue damage, which can result in decreased life expectancy or even mortality. According to the estimates from the International Diabetes Federation, 537.2 million adults (1 in 10) were breathing with diabetes in 2021. This figure is expected to escalate to 644 million by 2030 and 784 million by 2045. These figures indicate the

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increasing demand and place for advances in the treatment of diabetes in healthcare systems [2]. The majority of cases of diabetes can be broken down into three subtypes: type-1 diabetes (T1- D), type-2 diabetes (T2-D), and diabetes caused by pregnancy (GDM). Patients with type 2 diabetes develop resistance to insulin throughout the disease and will also lose the ability to produce sufficient amounts of this hormone at later stages. Early in the illness, hyperglycemia can be controlled by oral hypoglycemic drugs that increase insulin secretion, release or absorption; however, as the disease progresses, patients will ultimately need insulin injections. Patients with diabetes (type-1) have pathology in producing insulin and must rely solely on insulin from an external source to control their blood glucose levels. Insulin must be administered consistently to treat type 1 diabetes which can be done through multiple daily injections (MDIs) or continuous subcutaneous insulin infusion (CSII) with a pump. GDM is managed like type 2 diabetes; the condition manifests in pregnant women because of the interactions between insulin and placental hormones [3].

Health education and counselling of patients about self-management, taking the right medications on time, and awareness about early detection of complications can prevent the occurrence of ketoacidosis, nephropathy, retinopathy, cardiovascular disease, diabetic foot, or stroke [4]. In addition to using medications, controlling diabetes requires patients to adhere to a wide variety of self-care patterns for better compliance, which is practically not easy unless they are highly self-motivated. These behaviors include the following:

- Carefully scheduling meal options
- Counting carbohydrates
- Getting enough exercise
- Monitoring blood glucose levels
- Making adjustments to daily activities

Lifestyle changes should be the primary focus, and therapeutic decisions should be specific to the patient considering his medical history and other associated medical conditions [5,6].

The subject of artificial intelligence (AI) is advancing at a rapid rate. Intelligent algorithms are used extensively in data-driven systems and can be traced in published research. These methods support advanced exploration and offer individualized medical assistance. Data shows that many healthcare businesses employ artificial intelligence strategies [7,8]. The near-term projections suggest that a significant level of effectiveness in artificial intelligence-incorporated clinical training will be achieved. The primary reasons for this revolution are the meteoric rise in the information and data of patients currently accessible and the efficiency of intelligent methodologies that can handle and process this information. These two factors have contributed to creating applications and tools that can improve the efficiency of treatment of complex illnesses such as diabetes and carcinoma [9].

The management of diabetes has undergone a complete paradigm shift over the last ten years as a direct outcome of incorporating novel tools and technologies, like CGM devices and artificial pancreas (AP). There is a chance of exploitation of data obtained by employing these innovative methods, which should also be kept in check. Because of the exponential growth in the amount of data

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that can be obtained electronically from individuals who have diabetes, artificial intelligence (AI) is receiving increasing attention in this field [10]. Regulation of one's blood glucose level is essential to manage diabetes.

Maintaining a glycated haemoglobin (HbA1C) level of less than 7% as well as a preprandial plasma glucose level of 80-130 mg/dL and a postprandial plasma glucose level of less than 180 mg/dL, is the glycemic targets that are recommended for individuals with diabetes by the American Diabetes Association. By providing glucose readings in real-time and empowering people with diabetes to make well-informed decisions regarding their treatment, the technological advancement known as continuous glucose monitoring (CGM) has changed how diabetes is managed.

The first continuous glucose monitoring (CGM) device received approval from the Food and Drug Administration (FDA) in the United States in 2001. This device was called GlucoWatch Biographer [10]. This device collected glucose from the interstitial fluid using reverse iontophoresis and monitored glucose levels every 20 minutes for up to 13 hours. It also collected glucose from the blood. Despite this, the apparatus did not see widespread use because it had a low level of precision and needed to be more reliable. Over the past few years, C.G.M. technology has seen significant advancements, making several devices available for purchase [11]. These devices include, among others, the Dexcom G6, the Freestyle Libre and the Medtronic Guardian Connect. These devices make use of a miniature monitor that is positioned subcutaneously to accomplish the goal of identifying the glucose concentration that is present in the interstitial fluid. Real-time glucose readings, trend data, and high or low glucose level alerts are presented on a receiver or smartphone software that receives figures from the sensor. The receiver may be a standalone device or integrated into a smartphone. It has been demonstrated that individuals who have diabetes who use CGM technology can improve their glycemic control and can lower the chance of hypoglycemia compared to Non-CGM users

According to the findings of several studies, CGM has also been proven effective in reducing patients' HbA1C levels and increasing their overall quality of life [12,13]. In addition, it has been demonstrated that AI can provide helpful management tools to deal with incremental data repositories through complicated and refined methods. This literature review addresses the advancement in AI-aided glucose monitoring and management.

Methodology

Data collection

The purpose of the literature analysis was to investigate and analyse the function of continuous glucose monitoring that plays a role in efficiently controlling the blood glucose levels in diabetes. Finding, selecting, extracting, and putting together a summary of the data was done systematically. Using search terms like "continuous-glucose monitoring," "diabetes management tools," "CGM," "glycemic control," "Artificial intelligence in diabetes", "diabetes type 1," and "diabetes type 2," a search for pertinent studies was carried out in online databases such as PubMed, Cochrane Library, and

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Google Scholar. Only articles that were published between the years 2000 and 2022 were considered for this search.

Data cleaning and pre-processing

The titles and summaries of the studies were reviewed to determine whether or not they were pertinent, and duplicates were eliminated. After that, the relevant studies were examined to decide whether or not they fulfilled the inclusion and exclusion criteria. Studies that examined the influence of continuous-glucose monitoring on glycemic regulation in patients with type 1 or type 2 diabetes, compared CGM with other methods for managing diabetes, and reported on the efficacy and safety of CGM were all included in the current review. Studies not written in English, not peer-reviewed, and not performed on humans were omitted. When applicable, the data were subjected to narrative synthesis, which allowed for both the qualitative and quantitative synthesis of the information.

Evolution of continuous glucose monitoring

Glycemic recognition, a chemical or physical transducer, a wireless transmission element and a receiver are the typical components of a specific CGM system [14].

The glucose recognition element demonstrates a high sensitivity to glucose and is an essential component in the operation of the CGM.

The part that performs the role of the transducer is responsible for converting the glycemic concentration into a quantifiable analytical signal. In an ideal scenario, the indicator would be wirelessly transmitted to a handset, a mobile application or a specialized handheld device that incorporates definite algorithms to monitor glucose amounts or even an insulin drive [15].

CGM can be placed into two categories, namely optical and electrochemical sensors, depending on the transducer element it utilizes. In the last few decades, many attempts have been made to investigate the new technologies that will improve the conduction of CGM.

The first report of continuous monitoring of plasma glucose levels in human patients was made by Weller, et al., [16] in the 1960s. CGM is the result of a significant amount of work that has been put forth, much of which was motivated by the search for a mechanical pancreas. For instance, in 1963, Kadish utilised continuous real-time glycemic monitoring as the primary strategy to test closed-loop glycemic control [17,18].

Glycemic sensing expertise for continuous monitoring

Technology for the electrochemical detection of glucose

Electrochemical enzymatic interactions of glucose with glucose dehydrogenase or glucose oxidase (GOx) are the basis for most commercially available blood glucose assays [19]. The first generation of electrical glucose biosensors were manufactured based on the principle of enzyme-catalyzed O_2-oxidation. These biosensors were sensitive enough to detect glucose levels in the blood. However, the first-generation glucose biosensor faced significant challenges in its development [20,21]. The higher operational potential is

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needed for detecting hydrogen peroxide (H_2O_2), which oxidizes and generates high current densities. The other challenge is that in the absence of a redox mediator, the speed of the direct electron transportation from the $FADH_2$ centre of glucose oxidase (GOx) to the surface of the working electrode must be increased to have the desired impact on time. To solve the earlier problems, the second-generation glycemic biosensor implements a redox mediator, lessening the device's reliance on oxygen in the surrounding environment [22].

Consequently, the assessment can be performed at a reduced applied potentiality to sidestep the result of biological interferences [23]. Many publications have described how electrochemical detection technology can be used in CGM applications. For instance, microneedle-based CGM biosensors attract more attention because they cause less discomfort and less damage to the surrounding tissue [24-29]. In addition, devices built on electrochemical microneedles have the potential to perform glucose monitoring and therapy at the same time [30]. The nonenzymatic glycemic sensors have several benefits, including resistance to the effects of changes in their surrounding environment, ease and copiability of fabrication, cheaper cost and freedom from the constraints of oxygen (O_2) availability [25,31]. A study, for instance, described a nonenzymatic glycemic sensor based on nanoporous platinum as the catalytic substance and a wireless unit for continuous glucose monitoring (CGM) [32,33].

Technology for the optical detection of glucose

Instead of detecting changes in electrons, optical tracking technology relies on detecting changes in photons in the light [34], so it is a good scheme for continuous glucose monitoring as it permits faster and constant monitoring [35]. Surface plasmon resonance (SPR), Fluorescence, Near-infrared, Raman, Optical coherence tomography, and Fourier transforms near-infrared are some types of optical biosensors that can be classified based on the transducer systems that they use.

For instance, research introduced a fluorescence affinity hollow fibre sensor for transdermal fluorescence-based glycemic monitoring, the sensor contains dyed globules and concanavalin A. With response times ranging from 5 to 7 minutes, the fictitious sensor can monitor glycemic levels within the physiological series [36,37]. The Senseonics CGM sensor is a fluorescence-based glycemic sensing system that is intended for use in commercial applications. This system comprises an implantable glycemic sensor and a wearable transmitter that measures glucose levels in the interstitial fluid (ISF) [37]. Recent research by Sawayama and colleagues has resulted in the development of an implantable CGM that uses Fluorescence and contains a glycemic-responsive fluorescence pigment to continuously monitor blood glycemic concentrations for up to 45 days [38]. Because of its ease of use and relatively low price, SPR has garnered much attention in developing biosensors in recent years. The SPR-detecting technology operates based on variations in the refractive index brought about by interactions between glucose molecules and a surface plasmon wave. This is the core concept behind the technology [39,40].

Challenges: Most optical devices today are expensive and challenging to miniaturize. In addition, optical glycemic sensing knowledge has weak signal-to-noise ratios and typically requires invasive depth calibration to be accurate. The non-invasive optical glucose sensing technology does not have a charted algorithm model that satisfies the clinical requirements. This is because individual disparities such as skin thickness, fat, and blood volume come into play [15].

Patient perspectives on continuous glucose monitoring

Self-monitoring of blood glucose (SMBG) is important to strategize the diet plan, exercise, and treatment [42,43]. Self-monitoring of blood glucose is reportedly done by approximately 75 per cent of individuals with type 2 diabetes [44]. According to grade E-level experts, the American Diabetes Association suggests that SMBG "may be highly beneficial when altering diet, physical exercise, and medications" [45]. Patients who participated in qualitative research reported that using SMBG helps them manage their diabetes because it enables them to construct mental models and mark decisions regarding self-management [46,47]. In contrast, few studies show no enhanced patient satisfaction, lifestyle and well-being with SMBG [48].

PROs and QoL measures have been evaluated in several studies employing validated questionnaires [49-52]. These questionnaires include the Diabetes Treatment Satisfaction Questionnaire (DTSQ), the Diabetes Class of Life Clinical Trial Questionnaire, and the Hypoglycemia Fear Survey (HFS). Patients who used CGM reported a better quality of life and were more satisfied with their medication than those who used conservative self-monitoring of blood glucose (SMBG). Patients who used CGM in a study by Jendle and colleagues experienced significantly fewer indications of hypoglycemia and hyperglycemia, which improved their well-being and quality of life (QoL) [53,54]. In a study conducted by the Continuous Glucose Monitoring Study Group of the Juvenile Diabetes Research Foundation, adults diagnosed with type 1 diabetes who used CGM experienced an improvement in their quality of life and treatment satisfaction, in addition to a decrease in diabetes-related distress. Patients who used CGM have also reported a reduced fear of hypoglycemia and increased skills in diabetes self-management to regulate blood glucose in a better way [55]. However, some studies have documented difficulties associated with CGM, such as skin irritation, discomfort, and disruption of regular activities [56,57].

Some patients may oppose CGM due to the stigma affiliated with having to wear a medical device. According to the findings of research conducted by Tanenbaum, et al., a few patients reported feeling self-conscious about wearing a CGM device, which impacted their use. Some patients, on the other hand, may experience a sense of empowerment and report a feeling of more authority in diabetes management as a result of using CGM. In addition to the attitude of patients, there are also obstacles to CGM adoption that are practical. For instance, patients might need help accessing the technology, or it might not be readily available in their region, or their insurance might not support it. The technical elements of CGM, such as the interpretation of data and troubleshooting, can also be

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challenging for patients. Healthcare providers can play an essential role in addressing these concerns and barriers through patient education about CGM. Providers can collaborate with clients to develop tactics to overcome practical obstacles, such as negotiating health insurance or troubleshooting technical problems. These strategies can be acquired through a collaborative effort between patients and providers [58].

Limitations and future directions for continuous glucose monitoring

Various PH and temperature factors affect the equilibrium proportion of different molecular conformations. The slow interconversion between different molecular morphologies of the glucose molecules may be very important for detecting glucose in other body secretions, such as sweat. Temperature swings can sometimes lead to circumstances that are out of equilibrium. Because enzymes are used in the process, the test strips can only be used once or for a limited time before they become useless. This results in accumulated costs and trash as people with diabetes use multiple strips daily. These constraints can be overcome by developing new methods for detecting glucose that should focus on the molecule's physical properties rather than chemical properties.

Research being done in this area is centered on figuring out how to identify glucose through the skin or body fluids such as mucus, saliva and tears [15]. New technologies with improved sensitivity and dependability in detection are required to accomplish this goal. A paradigm shift in glucose monitoring would be possible with the development of non-invasive techniques for glucose detection. This would substantially improve the quality of life for diabetic patients [59-62]. Continuous glucose monitors are also highly beneficial to dieticians in determining specific responses to food, which can be quite variable as individual responses can differ significantly [63].

Bruen, et al., examined the most recent developments in glucose monitors for various body fluids and summarized the findings [64]. Recent developments in electrochemical sensing were reviewed and discussed by Wang, et al., and Lin, et al., [65]. They focused on critical challenges and recent advancements in the field [66]. McCaul, et al., conducted a comprehensive review of various technological developments and the associated challenges and possibilities, particularly emphasizing sweat analysis [67]. Kim, et al., researched the most recent developments in non-invasive technologies that use interstitial fluid and sweat [68]. Oliver, et al., examined and explained the history of the technologies utilized for glucose sensing [69].

Recommendations for future work

Future research and clinical applications for continuous glucose monitoring can focus on various fields, such as creating CGM devices that are more precise and easily dependable. This involves advancements in the sensor's stability, longevity, and precision. Developing non-invasive or slightly invasive C.G.M. devices would also help patients adhere to their treatment plans and experience less discomfort from the existing devices [70,71]. More research should be done on applying CGM in particular patient groups. This

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encompasses people with type 2 diabetes who are insulin-dependent, type 1 diabetic children, and diabetic pregnant women. Customizing treatment plans and enhancing clinical outcomes will be more if one knows advantages and restrictions in these groups [72]. Thirdly, it's essential to investigate how CGM can work with machine learning and artificial intelligence (AI) systems. This trend could result in more accurate predictions of glucose trends and patterns and personalized treatment strategies based on data specific to each patient [41].

Conclusion

The area of continuous glucose monitoring (CGM) is rapidly developing, and innovations are constantly being made. Future studies should concentrate on a few crucial areas to increase its efficacy and clinical utility. CGM has much promise to enhance diabetes management and clinical outcomes, yet issues must be resolved to broaden the adoption and increase access. Healthcare providers can provide better care and support their diabetic patients by keeping an update on recent research and CGM developments.

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