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Artificial Intelligence in Type II Diabetes Mellitus: Screening, Treatment, and Complication

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Abstract

Type II diabetes mellitus is one of the chronic metabolic diseases that are associated with insulin resistance. Type II diabetes mellitus incidence continues to increase each year and may cause various health complications, even death. Addressing early detection and appropriate treatment is important in decreasing the incidence of type II diabetes mellitus and improving the quality of life in diabetic patients. The potential of artificial intelligence in healthcare is expected to assist in screening, therapy management, and even detection of type II diabetes mellitus complications. Despite limited literature, this study aims to understand the benefit of AI in assisting health workers in screening and managing type II diabetes mellitus. Searches are conducted with search engines, such as PubMed, Science Direct, and Google Scholar, with the keywords "Artificial Intelligence" and "Diabetes Mellitus Type 2", as well as their synonyms. The search results in twenty English and Indonesian studies were published in the last ten years. These various studies found that many Artificial intelligence models developed to assist in screening, therapy management, and detect complications in patients with type II diabetes mellitus.

Introduction

Type II diabetes mellitus is a chronic metabolic disease causing insulin sensitivity disruption in body tissues and hyperglycemia. Type II diabetes mellitus is multifactorial, caused by genetic factors and lifestyle. The sedentary lifestyle that is commonly practiced by people today, along with excessive diet, plays a significant role in the occurrence of type II diabetes mellitus. According to the American Diabetes Association (ADA), the criteria for type II diabetes mellitus consist of several, namely when someone has symptoms of diabetes with blood sugar levels of more than 200 mg/dL; fasting blood sugar levels exceeding 125 mg/dL; HbA1c above 6.5%; and blood sugar on the oral glucose tolerance test (OGTT) of more than 200 mg/dL (Loscalzo *et al.*, 2022; American Diabetes Association, 2022).

The prevalence of type II diabetes mellitus in the world has continued to increase in the last two decades, estimated at around 30 million cases in 1985 and increasing to 415 million cases in 2017. Based on the World Health Organization (WHO), around 422 million people worldwide have diabetes, and the majority live in countries with low and middle economic status. The incidence of type II diabetes mellitus in Indonesians is also reported to continue to increase every year. According to Riskesdas data, in 2013, the number of people with type II diabetes mellitus was 1.5%. In 2018, it was 2%. In 2023, there was a significant increase of 12.2%, which means

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that in 100 people, 12.2 people have type II diabetes mellitus (Loscalzo *et al.,* 2022; Badan Penelitian dan Pengembangan Kesehatan. Riset Kesehatan Dasar 2013). Type II diabetes mellitus can cause impacts on various aspects of life that will result in a decrease in a person's quality of life. WHO reports that around 1.5 million people die from diabetes each year. Type II diabetes mellitus can cause various health complications in macrovascular and microvascular. Examples of macrovascular complications are cardiovascular disease, stroke, and also disorders of the peripheral blood vessels. Meanwhile, complications can occur in microvascular such as neuropathy, nephropathy, and retinopathy (Loscalzo *et al.,* 2022; American Diabetes Association, 2023).

Type II diabetes mellitus often experiences delays in diagnosis so that the patient's condition has reached a complication phase that can be life-threatening. Therefore, it is important to be able to predict by screening and establishing an early diagnosis in people at risk of developing type II diabetes mellitus. In addition to screening and early diagnosis, comprehensive therapy for patients with type II diabetes mellitus is also important. Currently, various challenges are found in providing therapy for patients with type II diabetes mellitus, which can come from patient factors, health worker factors, and also limitations of existing pharmacological treatment. The difficulty of complying with the given therapy regimen, modifying lifestyle, tolerance to the drugs given, access to health services that are hampered, and others are some of the factors that make therapy for patients with type II diabetes mellitus not easy (Loscalzo *et al.,* 2022; Dinavari *et al.,* 2023).

Artificial intelligence, or AI, is experiencing development and progress, especially in the 21st decade. AI has a complex meaning. It can be briefly defined as a technology that aims to create an intelligence algorithm that can imitate human intelligence. AI is being used in various fields to help human work, one of which is the health sector. AI is also considered to be able to assist in screening, therapy management, and detecting complications in patients with type II diabetes mellitus. Even so, few literature that discusses and deepens this matter. Therefore, the purpose of writing this literature is to comprehensively understand the role of AI in helping health workers conduct primary screening and therapy and prevent complications in patients with type II diabetes mellitus (Wu *et al.,* 2023).

Method

The search was conducted using the keywords "Artificial Intelligence" and "Diabetes Mellitus Type II", and their synonyms. The search engines used were PubMed, Science Direct, and Google Scholar. The studies used were English and Indonesian published in the last 10 years. In the literature search, 20 studies could be used in this review article.

Results and Discussions

Late diagnosis of diabetes can lead to complications and lower life expectancy, so early screening and diagnosis are vital. However, early diagnosis of diabetes is more difficult because it is generally asymptomatic, so many people go undiagnosed (Guan *et al.*, 2023). AI can help screen for diabetes in individuals who have high-risk factors for diabetes. Research by Joshi *et al.* (2021), using logistic regression and classification tree models to identify important factors of type II diabetes mellitus. Finally, five main risk factors were found to be related. Namely the number of pregnancies in women, glucose, family history, BMI, and age. After a validation test, the research model had a prediction accuracy of 78% (Joshi & Dhakal, 2021). A recent study by Kaufman *et al.* (2023) can even use speech patterns to detect type II diabetes with AI. With voice frequency analysis, voice changes inaudible to the human ear will pass through AI analysis. Often, a voice recorder on a telephone is the software needed to perform the analysis. It will examine speech melody, rhythm, pauses, and pitch. Particular symptoms have distinctive phonetic characteristics, such as the pronunciation of the vowel A for five seconds. The human voice can display up to 200,000 different characteristics. An AI algorithm can sift through these characteristics to identify specific vocal patterns that match certain symptoms. The AI will sift through voice recordings that last between six and ten seconds, looking for differences in pitch and intensity of the vocals. Combined with basic health data, such as age, gender, height, and weight, the program can gauge whether the speaker has type II diabetes (kaufman *et al.,* 2023).

A study by Li *et al.* (2021) used tongue color and texture as predictors of diabetes, with an accuracy of up to 99%. This study explains that the tongue can be a potential marker to help diagnose prediabetes and diabetes (Li *et al.*, 2021). A previous study by Shu *et al.* (2017) used the effect of facial texture in predicting diabetes mellitus based on specific facial areas with texture extractors. In this study, an accuracy of up to 99% was obtained with a support vector machine (Shu *et al.*,2017). A study by Pyrros *et al.* (2023) used AI to screen for diabetes using x-ray images. By using 'deep learning' methods on images and electronic health record data, researchers were able to develop a model to detect the increased risk of diabetes in a retrospective analysis. Every year, millions of Americans receive chest X-rays, and these images become part of the patient's medical record and can later be analyzed for diabetes or other conditions. The AI model was run on more than 270,000 x-ray images from 160,000 patients, with 'deep learning' methods determining which image features were most likely to predict a later diagnosis of diabetes. Chest X-rays are not a common way to detect diabetes, so the researchers used AI techniques to determine how and why the model made its decisions. It found that the location of fat tissue was vital in determining risk, with visceral fat in the upper body and abdomen associated with type II diabetes, insulin resistance, hypertension, and other conditions. When the AI model was applied to a separate group of nearly 10,000 patients, it predicted risk better than a simple model based only on clinical data. In some cases, chest X-rays warned of a high risk of diabetes as early as three years before the patient was finally diagnosed (Pyrros *et al.*, 2023).

The incidence of type II diabetes mellitus as a non-communicable disease continues to increase from year to year. This chronic disease is influenced by various factors, including genetic factors and lifestyle. With the development of technology, more and more patients are utilizing AI, such as Chat Generative Pre-Trained Transformer (ChatGPT), a text-generating AI (TGAI), to find more information about their condition. A study by Hernandez CA, Vazquez Gonzalez AE, Polioanovskaia A, *et al.* (2023) showed that questions directed at TGAI provided fairly accurate answers. In the study, a group of experienced doctors asked various questions about type II diabetes mellitus to ChatGPT three times. All ChatGPT answers were summarized and categorized by the standard of care (latest guideline)', 'not appropriate', namely answers that contain elements of correct information but are incomplete or outdated, and 'unreliable' based on the assessment of two experienced doctors. A total of 70 questions, such as 'Can type II diabetes cause increased urination frequency?' were answered by ChatGPT, with an accuracy rate of 98.5%. Of the 70 questions, the question categorized as 'inappropriate' was 'Can stress affect blood glucose levels?'. The results follow a previous study by Haver *et al.* with an accuracy rate of 88%. The accuracy rate achieved by the TGAI application is higher than a regular search engine. However, TGAI requires further processing to improve accuracy.[15]

In addition, a study by Chen *et al.* (2022) was conducted in China due to limited access to health facilities so patients experience obstacles in receiving diabetes education. The study examined the effect of mobile phone applications on the knowledge of type II diabetes mellitus patients who will start treatment with premixed insulin. A mobile phone-based application called the Lilly Connected Care Program (LCCP) which functions as an educational program about diabetes was used by 9,426 patients with uncontrolled HbA1c for 12 weeks. The application contains a 'Daily Quiz' menu and 60 videos and articles about diabetes. After 12 weeks, HbA1c levels decreased from 9.8 ± 1.5% (84 ± 16.4 mmol/mol) to 7.4 ± 1.2% (57 ± 13.1 mmol/mol), and 36% of patients achieved HbA1c levels <7%. In addition, the number of patients experiencing hypoglycemia decreased from 10.1% to 4.4% (Chen *et al.*, 2023).

Nutritional intake also plays a vital role in blood sugar management in adult patients with type II diabetes mellitus. A study in Korea by Lee *et al.* (2023) divided 295 overweight and obese patients into three groups. The first group only received routine therapy/care, the second group only used a digital platform, and the third group used the platform. It was accompanied by advice from medical personnel and combined with continuous glucose monitoring (CGM) periodically. Participants in groups B and C were given a glucometer, a sphygmomanometer, a scale equipped with bioelectrical impedance analysis, and a watch-shaped pedometer that could be connected to the platform via Bluetooth. An AI program called FoodLens was used to photograph the food consumed by patients. It can assess calories and other nutritional data from various foods in the photo and then integrate with the platform. Group C participants were also equipped with a CGM device that was used for 1 week every 3 months and received feedback via SMS from medical personnel. The study showed that after 24 weeks, the decrease in HbA1c levels was higher in group B (−0.32 ± 0.58%) and group C (−0.49 ± 0.57%) than in group A (−0.06 ± 0.61%). After 48 weeks, groups B (−0.28 ± 0.56%) and C (−0.44 ± 0.62%) continued to experience a higher decrease than group A (0.07 ± 0.78%). In addition, at week 48, group C experienced a significant weight loss compared to group A (Lee *et al*., 2023). Research by Zeevi *et al*. (2015) found that there was a high level of blood sugar variability in the same diet. The study created a machine learning algorithm that integrated diet, blood sugar parameters, anthropometry, physical activity, and gut microbiota. The algorithm was used in 100 participants (31% with HbA1c >= 5.7% and 3% with HbA1c >= 3%) and effectively decreased post-prandial blood sugar (Zeevi *et al.,* 2015).

Several applications have been designed to facilitate the monitoring of diabetes mellitus, a chronic disease that has become the center of attention in health technology. Health technology provides a series of features, including monitoring diabetes conditions, creating a communication medium between patients and medical staff, enabling remote monitoring, recording and maintaining medical history, and increasing patient knowledge of the disease. An intelligent mobile diabetes management system (SAED) is designed to improve self-management, focusing on diabetes mellitus. The SAED system consists of three components, namely the user component (mobile patient/healthcare provider), the intelligent diabetes management component, and the diabetes educational module component (Diabetes educational module).

The user component functions to record blood sugar measurement results using a particular tool connected to the user's smartphone via Bluetooth. The data will be sent to the SAED cloud server accessed by the clinician concerned so that monitoring and communication can be done remotely. The diabetes management intelligence component functions as a system that helps to determine clinical decisions for clinicians by providing data from patients related to their current medical history. The diabetes education module aims to improve the knowledge of patients with diabetes to facilitate better self-management. A case-control study conducted by Alotaibi *et al*. (2016) showed that the intervention group with the SAED system experienced a significant decrease in HbA1c levels (7.85 ± 0.70) within 6 months compared to the control group, which experienced an increase in the average value (8.68 ± 1.54). Overall, the SAED system offers a solution to improve the quality of life of people with diabetes mellitus effectively and at low cost (Alotaibi *et al.,* 2016).

The currently popular method of monitoring blood sugar levels is the continuous glucose monitoring (CGM) biosensor. Jin *et al*. (2023), have made the latest innovation by combining AI and CGM biosensors to obtain individual-focused health services. CGM biosensors enable real-time monitoring of a person's blood sugar levels, reduce the pain obtained from capillary blood sugar examinations, and capture a holistic, individualized glycemic control model that facilitates lifestyle changes and personalized therapy. CGM systems generally consist of glucose recognition elements, physical or chemical transducer elements, wireless transmitter elements, and receivers. Glucose detection technology in CGM systems can be carried out electrochemically, optically, and using tools.

Artificial Intelligence can be used in closed-loop control algorithms or artificial pancreas systems, glucose prediction algorithms based on CGM biosensors, and CGM biosensor calibration algorithms. In artificial pancreas systems, AI can be incorporated into insulin pumps worn or smartphones that will function to calculate insulin doses accurately based on real-time measurements and differences in values with previous measurements. In addition, AI will also create an algorithm that can provide information or advice according to the knowledge of experts (practitioners or diabetes experts) to regulate insulin administration. Another function of the AI algorithm is to provide glucose level predictions that can be used to achieve glycemic balance. The calibration algorithm functions to prevent calculation errors that can result in hypoglycemia or hyperglycemia. The combination of AI with CGM biosensors offers convenience in controlling glucose levels in the body for people with diabetes mellitus. AI can be used in closed-loop control algorithms or artificial pancreas systems, glucose prediction algorithms based on CGM biosensors, and CGM biosensor calibration algorithms. In the artificial pancreas system, AI can be incorporated into a wearable insulin pump or smartphone that will calculate the insulin dose accurately based on real-time measurements and differences in values with previous measurements. In addition, AI will also create an algorithm that can provide information or advice according to the knowledge of experts (practitioners or diabetes experts) to regulate insulin administration. Another function of the AI algorithm is to predict glucose levels to achieve glycemic balance. The calibration algorithm functions to prevent calculation errors that can result in hypoglycemia or hyperglycemia. The combination of AI with CGM biosensors offers convenience in controlling glucose levels in the body for people with diabetes mellitus (Jin *et al.*, 2023). The quality of life of people with type II diabetes mellitus depends on the ability to predict, diagnose, and provide appropriate management of complications (both acute and chronic). Here are some potential advances in AI for early detection of complications in type II diabetes mellitus.

Flash glucose monitors (FGMs) and continuous glucose monitors (CGMs) are AI technologies used to detect and control hypoglycemia and hyperglycemia in patients with type II diabetes mellitus. Artificial intelligence has been commercially available and has shown potential in managing blood glucose effectively, not only in type 1 diabetes mellitus but also in type II diabetes mellitus requiring insulin. Evaluation of glycemic fluctuations with CGMs such as FreeStyle Libre (Abbott Diabetes Care, Alameda, CA, USA) has been shown to improve glycometabolic control and short-term oscillations in patients requiring multiple insulin administrations. Continuous glucose monitoring (CGM) is more effective than FGM in preventing hypoglycemia. When combined with an insulin pump, CGM systems offer the potential for closed-loop insulin systems, also known as artificial pancreas systems. For example, Diabeloop technology (Diabeloop SAS, Grenoble, France) promises to manage type II diabetes mellitus by reducing overall healthcare costs and delivering insulin to individuals who need it (Behera, 2021). An autonomous artificial intelligence (AI) known as IDx-DR (Digital Diagnostics, Coralville, IA, United States) is designed to diagnose diabetic retinopathy and macular edema in real time at the point of care. The initial development of IDx-DR occurred at the University of Iowa as the Iowa Detection Program (IDP).

IDx-DR is the first autonomous artificial intelligence system to receive commercial authorization from the U.S. Food and Drug Administration (FDA). The study that formed the basis for IDx-DR approval was conducted in a primary care setting using operators with no prior experience in retinal imaging. Data collected by certified retinal photographers (OCT) and four wide-field stereoscopic fundus images were compared to patient outcomes. The images were evaluated by an autonomous reading center that developed the Early Treatment for Diabetic Retinopathy Study (ETDRS), the patient outcome reference standard applied to all DR management trials. The system is designed to identify clinically significant or center-related diabetic macular edema (DME), or an ETMDS grade of 35 or higher. IDx-DR has been certified in Europe as a class IIa medical device (Grzybowski & Brona, 2021).

In Caucasian, North African, and Sub-Saharan populations, the IDP has demonstrated positive results. The IDP algorithm and human raters analyzed images associated with 3640 participants in the Nakuru Eye Study conducted in Kenya. Human raters and the IDP agreed that the images were of inadequate quality 334 times. Twenty cases were identified by human raters as having poor image quality, whereas the IDP analysis determined that the images were evaluable and free of diabetic eye disease (DED). The IDP achieved a specificity of 70.0% and a sensitivity of 86.7% when patients were not evaluable, which was similar to the performance of human raters. Importantly, human raters did not identify any of the false-negative results as indicating sight-threatening DED (Grzybowski *et al.*, 2020).

In addition, IDX-DR was recently validated in a practical setting within the Dutch diabetes care system. Eighty-four percent of 1410 patients were deemed to be of adequate quality by three independent human raters, compared with 66.3% for the IDX-DR system; however, there were concerns regarding the functionality of the re-imaging alert built into the system. Images were evaluated by study experts using a combination of the ICDR and EURODIAB scoring systems. The sensitivity/specificity of IDX-DR was 91%/84% by EURODIAB and 68%/86% by ICDR. The significant performance gap between EURODIAB and ICDR can be attributed to the ICDR scale criteria that classify one bleed as having at least one major complication. Reconsidering it, the authors observed that the sensitivity and specificity of IDX-DR would be 96% and 86%, respectively. The population studied showed a low prevalence of DR, a characteristic associated with effective diabetes management and regular screening (Van der Heijden, 2018).

Developed in Portugal, the RetmarkerDR software has been used locally for diabetic retinopathy (DR) screening for several years. In 2011, it was integrated into a human-rater-based DR screening program already running in a Portuguese center. In this case, Retmarker is used for initial classification into “disease” or “no disease,” thus designating the “disease” subgroup for evaluation by human raters. RetmarkerDR implements a machine learning (ML) algorithm based on features. The primary uniqueness of RetmarkerDR lies in its ability to compare current images with those previously evaluated. It allows us to determine whether disease progression has occurred. In addition, the software can identify the rate of manifestation of new and pre-existing microaneurysms; it is referred to as the “microaneurysm change rate.” It appears to be a prospective marker for progression to diabetic maculopathy and worsening DR, as intravitreal ranibizumab therapy for diabetes mellitus is associated with a decreased rate of microaneurysm change. Intravitreal implants containing dexamethasone have also been associated with a lower rate of microaneurysm change in patients with diabetes. However, this is a subject that requires substantial additional research (Grzybowski *et al.*, 2020).

In a comprehensive review of the prospective application of AI-based DR screening tools in national DR screening in the UK, RetmarkerDR was used for analysis.24 From over twenty thousand patients screened at a single center in London, Tufail *et al.* analyzed two images per eye, one focused on the macula and the other on the disc. A comprehensive evaluation of the economic efficiency and screening efficacy of three ARIAS - RetmarkerDR, EyeArt, and iGradingM - was performed for this study. The obtained sensitivities for proliferative retinopathy (97.9%), referable retinopathy (85.0%), and any retinopathy (73.0%) were in contrast to the results of audited human assessors. There were 47% false positives (Grzybowski *et al.*, 2020).

Currently, AI is used to create a risk factor algorithm that combines physical examination parameters and demographic information to calculate the likelihood of a patient developing a diabetic foot ulcer with an accuracy of 79.8%.26 The primary purpose of using AI is to identify the likelihood of a patient developing a diabetic foot ulcer. The applied technologies are thermography and multispectral imaging. The use of AI in the prevention of diabetic foot ulcers is currently under development. Currently, no adequate data can be used to diagnose prevention in patients at high risk of diabetic foot ulcers. Most data currently under development is from Manchester Metropolitan University, with a total of 11 thousand images, but the number of images is still insufficient to diagnose prevention (Huang *et al*., 2022).

Current diagnostic examinations for diabetic peripheral neuropathy (nerve conduction velocity examination, quantitative sensory examination, skin biopsy) are less efficient because they are time-consuming and have low specificity. AI can be diagnosed with three types. They are qualitative and quantitative physiology and anatomical examinations. Qualitative examinations can be in EuroQol-5 Dimension (EQ5D) health-related quality-of-life examinations. Artificial Intelligence plays a role in quantitative physiological examinations to stratify the level of severity at different places at the same time. Anatomically, AI with magnetic resonance imaging and ultrasound images of peripheral nerves can create biomarkers of diabetic peripheral neuropathy pain based on functional connectivity and blood flow in the central nervous system. However, Corneal confocal microscopy is more effective than AI examinations because it has faster sensitivity and results and is more non-invasive (Huang *et al*., 2022).

Conclussions

Artificial Intelligence (AI) has significantly influenced the management of type II diabetes mellitus with success in screening, diagnosis, therapy management, and complication detection. With various AI models, such as logistic regression, color analysis, and blood sugar monitoring technology, high accuracy in detecting risk factors and symptoms of the disease has been achieved. In diabetes management, AI plays a role in health education, nutrition monitoring, and the closed-loop control system developed for insulin dosing. Mobile applications and digital education programs help improve patient understanding and control HbA1c levels. The contribution of AI in detecting complications opens up the potential for early prevention and intervention. Although challenges such as validation and safety need to be overcome, the great potential of AI in improving quality of life and reducing the risk of complications shows a positive direction toward AI integration in chronic disease management.

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