ORIGINAL ARTICLE

Retrospective Observational Study for Assessment of Prevalence of Hypoglycemic Episode by Continuous Glucose Monitoring in Patients of Type 2 Diabetes Mellitus

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Abstract

Introduction: Type 2 diabetes mellitus (T2DM) is a progressive metabolic disorder characterized by insulin resistance and β-cell dysfunction, leading to chronic hyperglycemia and complications. Despite therapeutic advances, hypoglycemia remains a major challenge, especially in patients on insulin or secretagogues. Continuous glucose monitoring (CGM) provides comprehensive data on glucose variability, time-in-range (TIR), and time-below-range (TBR), offering superior insights compared to traditional monitoring. This study aimed to assess the prevalence and characteristics of hypoglycemia in T2DM using CGM.

Materials and methods: A retrospective observational study was conducted at a tertiary care center in India between April 2023 and October 2024. A minimum sample size of 46 was estimated, and 50 patients were included. Inclusion criteria: Adults >18 years with T2DM, HbA1c >8%, undergoing CGM, and consenting. Exclusion criteria: HbA1c <8%, nondiabetic steroid users, critically ill patients, or those unwilling to participate. CGM was used to detect hypoglycemia (<70 mg/dL). Episodes were classified as symptomatic or asymptomatic. Associations with different antidiabetic drugs and combinations were evaluated statistically.

Results: Demographics: mean age was 64.2 ± 7.9 years; 42% were aged 61–70 years. Mean body mass index (BMI) was 24.9 ± 3.0 kg/m^2, with 46% overweight. Hypoglycemia prevalence: 80% (40/50) experienced hypoglycemia; of these, 60% were asymptomatic and 40% symptomatic. Drug associations: metformin: not significantly associated ($p = 0.29$). Dipeptidyl peptidase-4 (DPP-4) inhibitors: significantly associated with hypoglycemia ($p = 0.003$). Sulphonylureas: trend toward increased risk, not statistically significant ($p = 0.76$). Sodium–glucose cotransporter-2 (SGLT-2) inhibitors: no significant association ($p = 0.18$). Insulin: high incidence of hypoglycemia, though not statistically significant ($p = 0.26$). Combination therapies: sulphonylureas + insulin: 62.5% of hypoglycemic patients were on this combination, compared to 50% in the nonhypoglycemic group ($p = 0.47$). Although not statistically significant, the high incidence suggests an additive risk. Sulphonylureas + DPP-4 inhibitors: 25% of hypoglycemic patients were on this regimen compared to 50% in the nonhypoglycemic group ($p = 0.12$). The incidence indicates that when combined, risk may vary depending on coexisting therapies.

Discussion: This study revealed a strikingly high prevalence of hypoglycemia (80%) in poorly controlled T2DM patients, with asymptomatic episodes being more frequent. CGM proved crucial in detecting silent hypoglycemia, which carries the risk of severe complications. Metformin showed no significant risk, confirming its safety. DPP-4 inhibitors, usually considered low risk, were significantly associated here, likely due to concomitant therapy. Sulphonylureas and insulin showed high incidence rates consistent with the literature, though statistical significance was not reached due to small sample size. Importantly, combination therapy with sulphonylureas and insulin was associated with a substantial proportion of hypoglycemic cases (62.5%), highlighting the need for careful use.

Limitations: Small sample size, single-center, limiting generalizability.

Conclusion: Hypoglycemia is highly prevalent in T2DM patients with poor control, especially asymptomatic forms, emphasizing the role of CGM. While metformin remains safe, insulin, sulphonylureas, and combination therapies (particularly sulphonylureas + insulin) markedly increase hypoglycemia risk.

Clinical implications: Routine CGM can detect hidden hypoglycemia and guide therapy. Drug regimens, particularly combinations, must be individualized. Elderly patients on insulin/secretagogues need close monitoring.

Future directions: Larger multicenter studies are needed to clarify long-term implications and refine therapeutic strategies.

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Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic condition characterized by insulin resistance and progressive pancreatic β-cell dysfunction. This results in hyperglycemia, significantly increasing the risk of microvascular and macrovascular complications. According to the International Diabetes Federation (IDF), approximately 537 million adults worldwide were affected by diabetes in 2021, with T2DM accounting for the vast majority of cases. This number is expected to rise to 783 million by 2045.[1] The pathogenesis of T2DM involves complex interactions between genetic and environmental factors, including obesity, physical inactivity, and dietary habits.[2] The condition often remains asymptomatic for years, leading to delays in diagnosis and early onset of complications. Optimal glycemic control is fundamental to preventing the acute and long-term complications of diabetes. Glycemic control is traditionally measured using glycated hemoglobin (HbA1c), which provides an average of blood glucose levels over the preceding 2–3 months. The target HbA1c for most patients is <7%, though individualized goals are recommended based on age, comorbidities, and the risk of hypoglycemia.[3] Emerging evidence emphasizes the significance of maintaining time-in-range (TIR), a metric provided by continuous glucose monitoring (CGM) systems, which tracks the percentage of time glucose levels remain within the target range of 70–180 mg/dL.[4] Maintaining a higher TIR is associated with reduced complications and improved quality of life.[5] Despite advances in diabetes care, hypoglycemia remains a significant challenge in managing T2DM. Traditional methods for monitoring glucose, such as fingerstick blood glucose testing,

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provide only snapshot readings, limiting their utility in capturing dynamic glucose fluctuations and identifying asymptomatic hypoglycemia. Continuous glucose monitoring (CGM) (Fig. 1) has emerged as a revolutionary tool, offering real-time insights into glycemic patterns.[6] CGM provides detailed metrics such as TIR, time below range (TBR), and glycemic variability (GV), enabling healthcare providers to optimize treatment strategies and reduce hypoglycemia risk.[7]

This study aims to evaluate the prevalence and characteristics of hypoglycemic episodes in T2DM using CGM data, bridging gaps in knowledge regarding real-world application and impact. By exploring CGM's potential, the study seeks to contribute to individualized diabetes management and improved patient outcomes.

Materials and Methods

Study Setting and Study Population

The study is conducted in a tertiary health care center and involves both urban and rural populations in India.

Sample size

$$N_0 = Z^2pq/e^2$$

N_0 is the sample size, Z^2 is the abscissa of the normal curve that cuts off area α at the tails; (1−α) equals the desired confidence level of 95%; *e* is the desired level of precision, *p* is the estimated proportion of an attribute that is present in the population, and *q* is (1−*p*). The value for *Z* is found in statistical tables, which contain the area under the normal curve, e.g., *Z* =1.96 for 95% level of confidence.

The sample size for the study = $(1.96)^2 \times 0.38 \times (1-0.38)/(0.14)^2$
= $3.84 \times 0.38 \times 0.62/0.0196$
= 0.905/0.0196
= 46.17

46 or more measurements/surveys are needed to have a confidence level of 95% that the real value of 38% is within ± 14% of the measured/surveyed value. *p* = 38% (proportion of diabetics with HbA1c ≥ 8%), *e* =14% margin of error, sample size =46. All indoor patients having diabetes mellitus meeting the inclusion criteria and attending medical services at this tertiary hospital during the study period.

Period of Study

This study included all patients who came to the hospital over 18 months, from 5th April 2023 to 5th October 2024, in whom CGM was indicated and performed as part of the treatment protocol.

Inclusion Criteria

All stable patients admitted with an age >18 years, both male and female.

- Diagnosed with diabetes mellitus (type 2) with unsatisfactory glycated Hb (HbA1c) >8%.
- Patients who were on CGM monitoring.
- Willing to participate.

Exclusion Criteria

- Patients with HbA1c below 8%.
- Nondiabetic patients who are on steroid therapy.
- Not willing to participate.
- Critically ill patients.
- Patients not able to provide consent.

Results

- *Demographics*: Mean age was 64.2 ± 7.9 years; 42% were aged 61–70 years (Table 1). Mean BMI was 24.9 ± 3.0 kg/m^2, with 46% overweight (Table 2).
- *Hypoglycemia prevalence*: 80% (40/50) experienced hypoglycemia; of these (Table 3 and Fig. 2), 60% were asymptomatic and 40% symptomatic (Table 4 and Fig. 3).
- *Drug associations*:
  - *Metformin*: Not significantly associated ($p = 0.29$) (Table 5 and Fig. 4)
  - *Dipeptidyl peptidase-4 (DPP-4) inhibitors*: Significantly associated with hypoglycemia ($p = 0.003$) (Table 6 and Fig. 5).
  - *Sulphonylureas*: Trend toward increased risk, not statistically significant ($p = 0.76$) (Table 7 and Fig. 6).
  - *SGLT-2 inhibitors*: No significant association ($p = 0.18$) (Table 8 and Fig. 7)
  - *Insulin*: High incidence of hypoglycemia, though not statistically significant ($p = 0.26$) (Table 9 and Fig. 8).

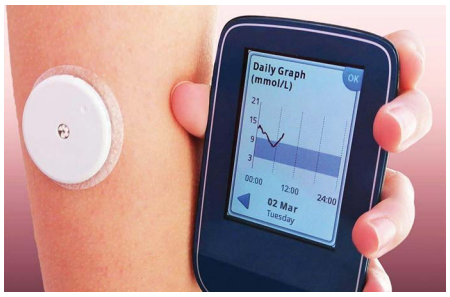

Fig. 1: Continuous glucose monitoring system

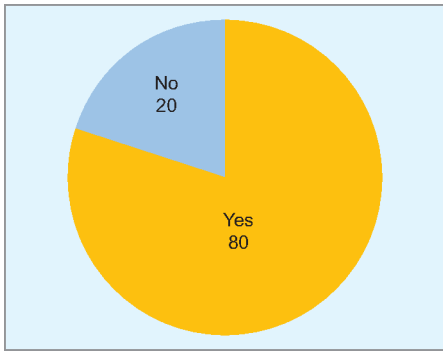

Fig. 2: Hypoglycemia distribution among study participants

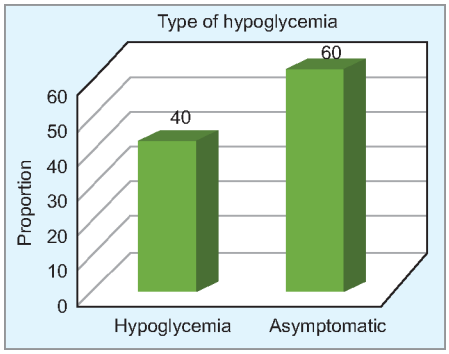

Fig. 3: Types of hypoglycemia among study participants

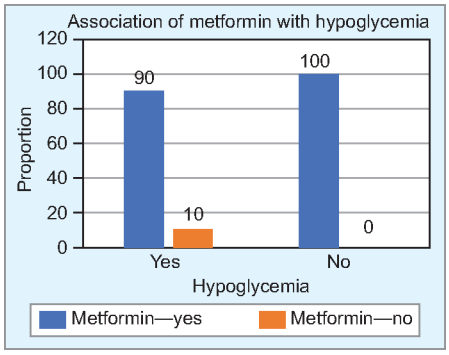

Fig. 4: Association of metformin with hypoglycemia among study participants

Table 1: Age distribution of the study participants (*N* = 50)

Age (years)	*Frequency (n)*	*Percentage (%)*
50–60	19	38.0
61–70	21	42.0
71–80	9	18.0
81–90	1	2.0
Total	50	100.0

The mean (SD) age of the study participants was 64.2 (7.9) years

Table 2: Body mass index distribution of the study participants (*N* = 50)

Body mass index (kg/m^2)[&]	*Frequency (n)*	*Percentage (%)*
Normal (18.5–24.9)	24	48.0
Overweight (25.0–29.9)	23	46.0
Obese (≥30)	2	4.0
Total	50	100.0

[&]WHO BMI classification; mean (SD) BMI of the study participants is 24.9 (3.0) kg/m^2

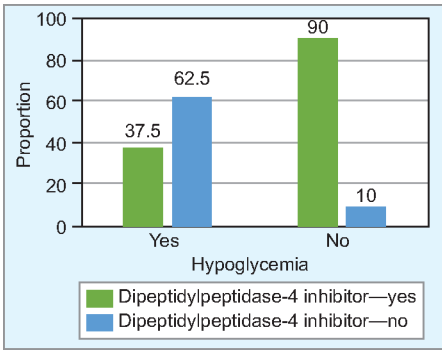

Fig. 5: Association of dipeptidyl peptidase-4 inhibitor with hypoglycemia among study participants

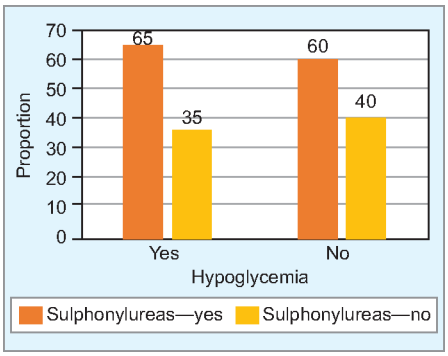

Fig. 6: Association of sulphonylureas with hypoglycemia among study participants ($N = 50$)

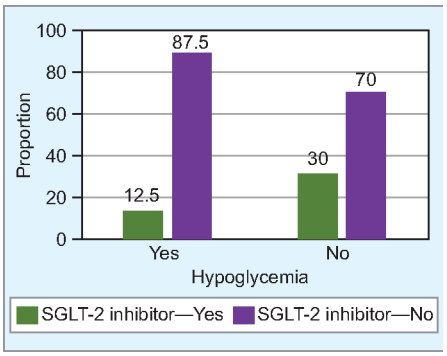

Fig. 7: Association of SGLT-2 inhibitor with hypoglycemia among study participants

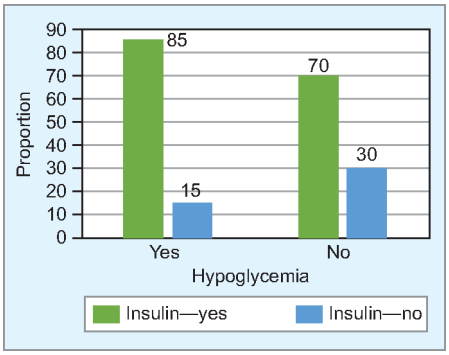

Fig. 8: Association of insulin with hypoglycemia among study participants

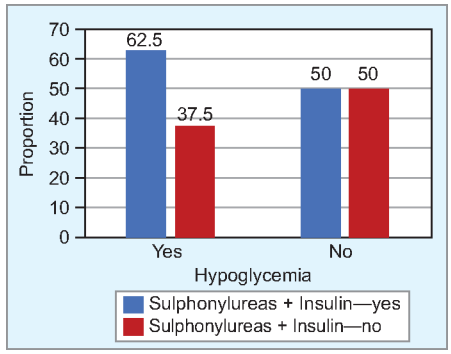

Fig. 9: Association of sulphonylureas plus insulin with hypoglycemia among study participants

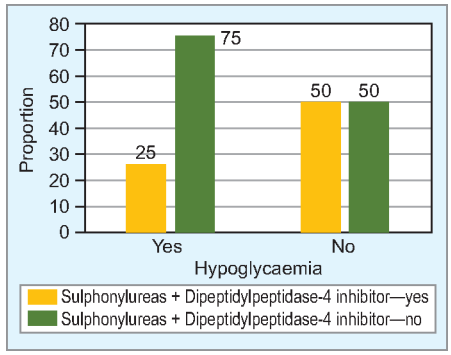

Fig. 10: Association of sulphonylureas plus dipeptidyl peptidase-4 inhibitor with hypoglycemia among study participants

Table 3: Hypoglycemia distribution of the study participants ($N = 50$)

Hypoglycemia	*Frequency (n)*	*Percentage (%)*
Yes	40	80.0
No	10	20.0
Total	50	100.0

Table 4: Type of hypoglycemia distribution of the study participants ($N = 40$)

Type of hypoglycemia	*Frequency (n)*	*Percentage (%)*
Symptomatic	16	40.0
Asymptomatic	24	60.0
Total	40	100.0

Table 5: Association of metformin with hypoglycemia distribution of the study participants ($N = 50$)

Metformin	*Hypoglycemia n (%)*		*p-value**
	Yes	*No*	
Yes	36 (90.0)	10 (100.0)	0.29
No	4 (10.0)	0 (0.0)	
Total	40 (100.0)	10 (100.0)	

*Signify Chi-squared test

- *Combination therapies*:
  - *Sulphonylureas + Insulin*: 62.5% of hypoglycemic patients were on this combination, compared to 50% in the nonhypoglycemic group ($p = 0.47$). Although not statistically significant, the high incidence suggests an additive risk (Table 10 and Fig. 9).
  - *Sulphonylureas + DPP-4 inhibitors*: 25% of hypoglycemic patients were on this regimen compared to 50% in the nonhypoglycemic group ($p = 0.12$). The incidence indicates that when combined, risk may vary depending on coexisting therapies (Table 11 and Fig. 10).

Discussion

Hypoglycemia and Its Associations

Hypoglycemia was a significant finding in this study, with 80% of participants reporting episodes of low blood glucose. Among those experiencing hypoglycemia, 60% were asymptomatic, while 40% reported symptomatic episodes. The high prevalence of asymptomatic hypoglycemia raises concerns regarding the risk of severe hypoglycemic episodes, particularly in older adults who may not perceive the warning signs. Research conducted by Bremer et al. revealed that many older individuals with type 2 diabetes exhibit considerable unawareness of hypoglycemia. This lack of awareness does not appear to stem from changes in neuroendocrine counterregulation and may increase the likelihood of experiencing severe hypoglycemia, which is often reported in this group. Furthermore, the coexistence of unawareness of hypoglycemia and diminished cognitive abilities is an important consideration.[8]

The association between hypoglycemia and different classes of antidiabetic medications was examined. Metformin use was not significantly associated with hypoglycemia ($p = 0.29$), which is consistent with existing literature suggesting that metformin has a low risk of causing hypoglycemia due to its insulin-independent mechanism of action.[9] However, DPP-4 inhibitors showed a significant association with hypoglycemia ($p = 0.003$), suggesting that their use might increase the risk in certain populations, but this could also be due to concurrent use of other medications such as sulphonylureas and insulin for the treatment of uncontrolled diabetes. Florentin et al. found that DPP-4 inhibitors are considered safe and are unlikely to lead to low blood sugar or increased weight. They do not necessitate any dosage adjustments. These medications can also be given to individuals with chronic kidney disease, with appropriate dose modifications, and are suitable for older adults managing diabetes.[10]

Table 6: Association of dipeptidyl peptidase-4 inhibitor with hypoglycemia distribution of the study participants (*N* = 50)

Dipeptidyl peptidase-4 inhibitor	*Hypoglycemia n (%)*		*p-value**
	Yes	*No*	
Yes	15 (37.5)	9 (90.0)	0.003
No	25 (62.5)	1 (10.0)	
Total	40 (100.0)	10 (100.0)	

*Signify Chi-squared test

Table 7: Association of sulphonylureas with hypoglycemia distribution of the study participants (*N* = 50)

Sulphonylureas	*Hypoglycemia n (%)*		*p-value**
	Yes	*No*	
Yes	26 (65.0)	6 (60.0)	0.76
No	14 (35.0)	4 (40.0)	
Total	40 (100.0)	10 (100.0)	

*Signify Chi-squared test

Table 8: Association of SGLT-2 inhibitor with hypoglycemia distribution of the study participants (*N* = 50)

SGLT-2 inhibitor	*Hypoglycemia n (%)*		*p-value**
	Yes	*No*	
Yes	5 (12.5)	3 (30.0)	0.18
No	35 (87.5)	7 (70.0)	
Total	40 (100.0)	10 (100.0)	

*Signify Chi-squared test

Table 9: Association of insulin with hypoglycemia distribution of the study participants (*N* = 50)

Insulin	*Hypoglycemia n (%)*		*p-value**
	Yes	*No*	
Yes	34 (85.0)	7 (70.0)	0.26
No	6 (15.0)	3 (30.0)	
Total	40 (100.0)	10 (100.0)	

*Signify Chi-squared test

Table 10: Association of sulphonylureas + insulin with hypoglycemia distribution of the study participants (*N* = 50)

Sulphonylureas + Insulin	*Hypoglycemia n (%)*		*p-value**
	Yes	*No*	
Yes	25 (62.5)	5 (50.0)	0.47
No	15 (37.5)	5 (50.0)	
Total	40 (100.0)	10 (100.0)	

*Signify Chi-squared test

Table 11: Association of sulphonylureas + dipeptidyl peptidase-4 inhibitor with hypoglycemia distribution of the study participants (*N* = 50)

Sulphonylureas + dipeptidyl peptidase-4 inhibitor	*Hypoglycemia n (%)*		*p-value**
	Yes	*No*	
Yes	10 (25.0)	5 (50.0)	0.12
No	30 (75.0)	5 (50.0)	
Total	40 (100.0)	10 (100.0)	

*Signify Chi-squared test

Sulphonylureas, which are known to increase the risk of hypoglycemia, did not show a statistically significant association in this study (p = 0.76), though the trend suggested a higher proportion of hypoglycemia cases in those using sulphonylureas. According to research by Dalem et al., individuals currently taking sulphonylureas face a significantly higher risk of hypoglycemia compared to those only on metformin, with an adjusted hazard ratio of 2.50 (95% confidence interval of 2.23 to 2.82). Furthermore, this risk is even higher among patients with an estimated glomerular filtration rate below 30 mL/min/1.73 m^2, resulting in an adjusted hazard ratio of 4.96 (95% confidence interval: 3.76 to 6.55).[11] Similarly, sodium-glucose cotransporter-2 (SGLT-2) inhibitors and insulin use were not significantly associated with hypoglycemia (p = 0.18 and p = 0.26, respectively), although insulin users showed a high prevalence of hypoglycemic episodes. Zaccardi et al. reviewed multiple trials involving SGLT-2 inhibitors and found that while these medications effectively lowered blood sugar levels and body weight, canagliflozin, in particular, posed a higher risk of hypoglycemia compared to others. Both canagliflozin and dapagliflozin were linked to an increased likelihood of experiencing low blood sugar. Additionally, dapagliflozin was associated with a higher incidence of urinary tract infections, and all inhibitors raised the risk of genital infections.[12]

In a study, Salvo et al. performed a systematic review that included 10 different studies, encompassing a total of 6,546 participants. Among these, 4,020 were treated with DPP-4 inhibitors alongside sulphonylureas, and 2,526 received a placebo combined with sulphonylureas. The analysis indicated a risk ratio of 1.52 for hypoglycemia, with a 95% confidence interval ranging from 1.29 to 1.80. The number needed to harm (NNH) was determined as follows: 17 (with a 95% confidence interval of 11 to 30) for treatment lasting 6 months or less, 15 (95% confidence interval 9 to 26) for treatment durations between 6.1 and 12 months, and 8 (95% confidence interval 5 to 15) for treatments extending beyond one year. Additionally, subgroup analyses revealed no significant differences between full and low doses of DPP-4 inhibitors. The risk ratio for those on full doses was 1.66 (95% confidence interval 1.34 to 2.06), while the risk ratio for low doses did not achieve statistical significance, reported as 1.33 (95% confidence interval 0.92 to 1.94).[13] We also did not find a significant relation between DPP-4 inhibitors alongside sulphonylureas.

Limitations of Study

- *Small sample size*: The study included only 50 participants, limiting the generalizability of the findings to larger diabetic populations.
- *Single-center study*: Data were collected from a specific population, and findings may not be representative of broader, more diverse diabetic cohorts.

Conclusion

Clinical Implications

- The high prevalence of asymptomatic hypoglycemia suggests a need for routine glucose monitoring, especially in older adults, to prevent severe episodes.
- Medication selection should be individualized, particularly when prescribing DPP-4 inhibitors, sulphonylureas, or insulin in patients at risk for hypoglycemia.
- Continuous glucose monitoring (CGM) or flash glucose monitoring may help better track glycemic variability and guide treatment adjustments.

Future Directions

Larger, longitudinal studies are needed to validate these findings and assess the long-term impact of hypoglycemia on diabetes-related complications.

This study highlights the significant burden of hypoglycemia among individuals with diabetes, with a high proportion of asymptomatic cases posing an increased risk of severe events. While metformin remains a safe option, the use of DPP-4 inhibitors, sulphonylureas, and insulin should be carefully evaluated to minimize hypoglycemic risk. The findings underscore the importance of individualized diabetes management, regular glucose monitoring, and optimizing glycemic control strategies to improve patient outcomes.

References

1. International Diabetes Federation. IDF Diabetes Atlas. 10th edition. Brussels: International Diabetes Federation; 2021.
2. Powers AC, Niswender KD, Evans-Molina C. Diabetes mellitus: diagnosis, classification, and pathophysiology. In: Jameson JL, Kasper DL, Fauci AS, et al. (Eds). Harrison's Principles of Internal Medicine, 21st edition. New York: McGraw Hill; 2022. pp. 2850–2863.
3. American Diabetes Association. Standards of medical care in diabetes—2023. Diabetes Care 2023;46(Suppl 1):S1–S304.
4. Battelino T, Danne T, Bergenstal RM, et al. Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus. Diabetes Care 2019;42(8):1593–1603.
5. Beck RW, Bergenstal RM, Riddlesworth TD, et al. Validation of time-in-range as an outcome measure for diabetes clinical trials. Diabetes Technol Ther 2019;21(2):81–85.
6. Device for continuous glucose monitoring of blood sugar levels–CGM. (2026) [online] Available from: https://www.dreamstime.com/device-continuous-glucose-monitoring-blood-sugar-levels-cgm-image212233758 [Last accessed April, 2026].
7. Bergenstal RM, Klonoff DC, Garg SK, et al. Threshold-based insulin-pump interruption for reduction of hypoglycemia. Lancet Diabetes Endocrinol 2018;6(11):886–896.
8. Bremer JP, Jauch-Chara K, Hallschmid M, et al. Hypoglycemia unawareness in older compared with middle-aged patients with type 2 diabetes. Diabetes Care 2009;32(8):1513–1517.
9. DeMarsilis A, Reddy N, Boutari C, et al. Pharmacotherapy of type 2 diabetes: an update and future directions. Metabolism 2022;137:155332.
10. Florentin M, Kostapanos MS, Papazafiropoulou AK. Role of dipeptidyl peptidase 4 inhibitors in the new era of antidiabetic treatment. World J Diabetes 2022;13(2):85–96.
11. van Dalem J, Brouwers MCGJ, Stehouwer CDA, et al. Risk of hypoglycaemia in users of sulphonylureas compared with metformin in relation to renal function and sulphonylurea metabolite group: population based cohort study. BMJ 2016;354:i3625.
12. Zaccardi F, Webb DR, Htike ZZ, et al. Efficacy and safety of sodium-glucose co-transporter-2 inhibitors in type 2 diabetes mellitus: systematic review and network meta-analysis. Diabetes Obes Metab 2016;18(8):783–792.
13. Salvo F, Moore N, Arnaud M, et al. Addition of dipeptidyl peptidase-4 inhibitors to sulphonylureas and risk of hypoglycaemia: systematic review and meta-analysis. BMJ 2016;353:i2231.