International Journal of Research in Medical Sciences
Saboo B. Int J Res Med Sci. 2020 Feb;8(2):738-742
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20200033

Case Report

Role of ambulatory glucose profile in identifying and managing a patient with disparity between FPG, PPG and HbAlc levels: a case report

Banshi Saboo*

Department of Endocrinology, Diabetes Care and Hormone Clinic, Ahmedabad, Gujarat, India

Received: 20 December 2019
Accepted: 03 January 2020

***Correspondence:**
Dr. Banshi Saboo,
E-mail: banshisaboo@hotmail.com

ABSTRACT

This case report describes the management of a patient with mismatch/disparity between his Fasting Plasma Glucose (FPG)/ Postprandial Glucose (PPG) levels with that of Glycosylated Haemoglobin (HbA1c) levels. This 43-year-old male patient with Type 2 Diabetes Mellitus (T2DM) was presented with increased urination and tiredness, especially in the evening hours, along with a tingling sensation in bilateral feet on and off, with leg pain since past 4 months. The patient was obese with a family history of cardiovascular disease. In this patient, SGLT2 inhibitors were found to be effective in addressing glycaemic variability without triggering hypoglycaemic risk. Continuous glucose monitoring system aided in understanding the blood glucose fluctuations caused by the diet. This case study indicated that careful evaluation and appropriate management using Ambulatory Glucose profile would aid in preventing complications in such patients and improve the overall clinical outcomes.

Keywords: Ambulatory glucose profile, Continuous glucose monitoring, Glycosylated haemoglobin, Type 2 diabetes mellitus

INTRODUCTION

India, known as the 'diabetes capital of the world' faces an indefinite potential burden that diabetes may impose upon the country. Of this, Type 2 Diabetes Mellitus (T2DM) is becoming an escalating public health problem, often associated with genetic susceptibility, dietary shift, and rapid lifestyle changes.[1]

Uncontrolled diabetes increases the risk of micro and macrovascular complications.[2] Effective metabolic control can be achieved by a combination of regular blood glucose monitoring, good patient education, and appropriate treatment. The early detection and treatment of T2DM, in turn, can improve a person's Quality of Life (QoL), thereby reducing the risk of severe complications. The "glycemic pentad" which includes Fasting Plasma Glucose (FPG), Postprandial Glucose (PPG), Glycosylated Hemoglobin (HbA1c), glycemic variability and QoL plays an important role in diabetes management, especially in the Indian context.[3]

However, often diabetic patients present with a mismatch/ disparity between the levels of FPG or PPG with that of HbA1c. In such a case, the patient might have fluctuations in his blood glucose levels, widely known as glycemic variability. In other words, the glycemic variability refers to swings in blood glucose levels and includes both postprandial spikes in blood glucose as well as hypoglycemic events, both of which are considered as important risk factors for cardiovascular events in patients with DM.[4-6] The severity of hyperglycemia and glycemic variability are shown to contribute to the pathogenesis of complications

such as retinopathy, peripheral neuropathy, urinary albumin excretion, cardiovascular events, and overall mortality; but the HbA1c measurement reflects only a piece of these important variables.[7-14] Numerous studies also support the association of long-term glycemic variability with an enhanced risk of micro and macrovascular complications, independent of HbA1c levels.[14-16] Hence in such cases, appropriate treatment decisions would be a challenge for the clinicians.

The intra-day glycemic variability often observed in diabetes patients could be ascribed to deficiency of endogenous insulin and amylin secretion, lack of appropriate suppression of glucagon upon eating, and poor compliance to diet, exercise, and treatment.[4] Hence timely identification of the reason for the inconsistency between FPG/PPG with that of HbA1c level is pertinent for effective management.

The following case report describes the management of a patient with the disparity between his FBS/PPG and HbA1c levels.

CASE REPORT

Here authors present a male, 43-year-old Type 2 diabetes patient, who presented to author's clinic with complaints of increased urination and tiredness especially in the evening hours, along with a tingling sensation in bilateral feet on and off, with leg pains since past 4 months. Patient was a known case of T2DM for 5 years with obesity, and a family history of Cardiovascular Disease (CVD).

Patient was on glimepiride 1 mg qd., and metformin 500 mg bid. The blood glucose values were found to be the following: FBS: 128 mg/dL, PPG: 160 mg/dL and HbA1c: 8.2%.

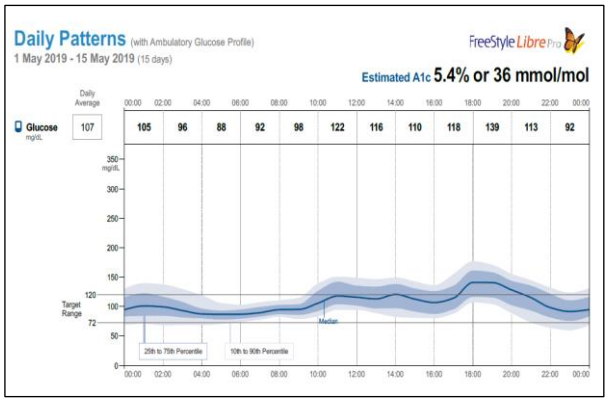

Figure 1: Ambulatory Glucose Profile (AGP) report based on the data obtained from CGM.

Though FPG and PPG levels were found to be in the optimal range, patient's HbA1c values were above the target, indicating a disparity between the values. This could be attributed to the glycemic variations that may have gone unnoticed. Consequently, the patient was recommended FreeStyle Libre Pro flash (Abbott, Alameda, CA) professional Continuous Glucose Monitoring system (CGM) to facilitate more frequent review of his blood glucose levels and to understand glycemic variability, if any.

From the above report, author can note the following points:

- On average, 62% of the time blood glucose levels were in the target range and ~31% of the time, blood glucose levels were above target range; for ~7% of the time blood glucose levels were below the target range (Figure 1).

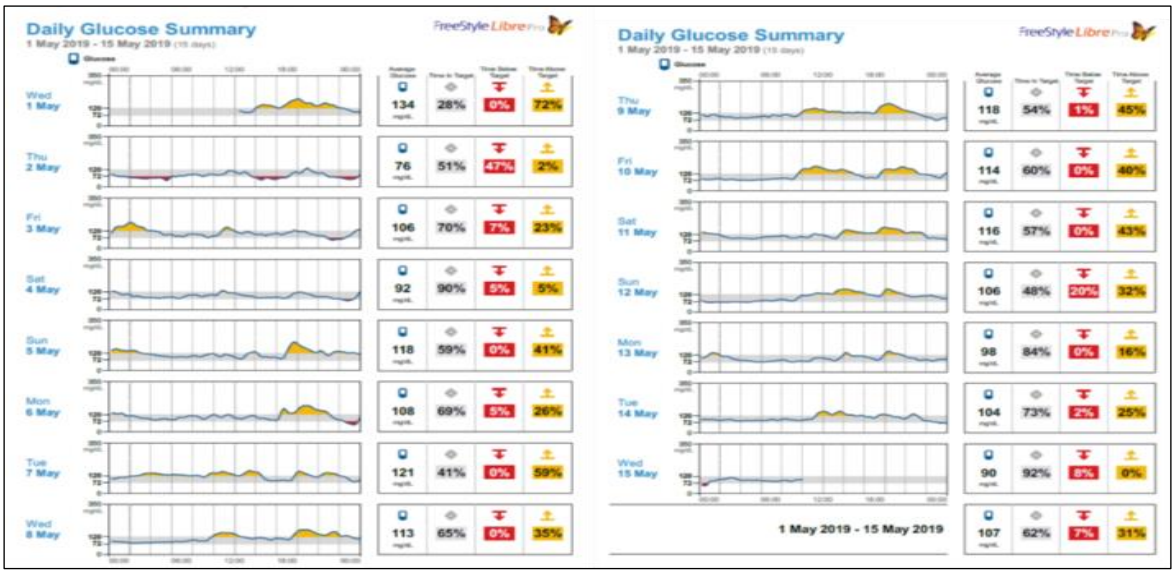

Figure 2: Daily glucose patterns.

- There was a potential risk of hypoglycemia in the night, specifically from 22:00 hrs to midnight.
- The graph showed some degree of hyperglycemia from 10:00 hrs onwards till 20:00 hrs.
- The median curve was stable during the first half of the day in contrast to the evening with curves corresponding with the meal timings - breakfast, lunch, and supper. However, the median stayed quite far from the baseline crossing over to hyperglycemia post 17:00 hrs. This could be secondary to high-calorie intakes at breakfast, lunch as well as supper.
- The Inter Quartile Range was relatively narrow between 04:00 to 09:00 hrs. The rest of the time IQR was much consistent with the movement of the median curve.
- The inter-decile range was relatively wider in the midnight between 12:00 to 04:00 hrs but was acceptable.

The complete glycemic profile obtained from the first AGP revealed an increased extent of glucose fluctuations (observed as hypoglycemic and hyperglycemic episodes). Subsequently, the patient's medications were changed based on the AGP. The use of glimepiride was discontinued, and the patient was recommended with dapagliflozin (10 mg) and metformin (1000 mg) qd with meals. The patient was recommended pregabalin (75 mg) and mecobalamin (1000 mg) at bedtime to address the symptoms of tingling sensation in the feet and pain in the leg, which were the symptoms of peripheral neuropathy. Further, the patient was counselled about the importance of diet control and regular physical activity (Figure 2).

DISCUSSION

This was a case of T2DM presenting with the disparity between FBS/PPBS and HbA1c levels. AGP report of this patient revealed evening spikes in blood glucose levels leading to high HbA1c. The reason might be a high carbohydrate evening snack that the patient might be consuming, hyperglycemia at evening or night hours, and/or high hepatic glucose output in the evening hours. In any which case, the patient was experiencing intra-day glycemic variability. Furthermore, the patient may be demonstrating good adherence to diet and therapy during blood glucose test routines, but not maintaining the same during other days. Therefore, it is necessary to address glycemic variability both by diet therapy as well as appropriate medications. Furthermore, part of the variability in HbA1c may be a consequence of differences in glycation rate, which was proposed as an explanation to the commonly encountered clinical problem of discrepancy between various glycemia measures that cannot be attributed to any other confounding factor.[17]

Studies suggest that the oral anti-diabetic drugs such as Dipeptidyl Peptidase-4 (DPP4) inhibitors and Sodium-Glucose Cotransporter-2 (SGLT2) are associated with lower risk of hypoglycemia, in comparison to other hypoglycemic drugs, and are more reliable in the management of situations characterized by comorbidities and polypharmacotherapy.[18] Hence, use of these drugs alone or in combination in T2DM patients would help in minimizing/delaying complications arising from glycemic variability.

The SGLT2 inhibitors are shown to have immediate glucose-lowering effects by promoting urinary glucose excretion, without altering insulin level, and are indicated to improve glycemic control in T2DM patients. A randomized study evaluated the effect of treatment with empagliflozin 10 mg or 25 mg versus placebo for 28 days on PPG and 24-h glucose variability in Japanese T2DM patients with baseline HbA1c of 7.9%. A significant adjusted mean difference at both day 1 and 28 in change from baseline in AUC1-4h for PPG and change from baseline in 24-h mean glucose was noted, versus placebo. Percentage of time with glucose ≥70 to <180 mg/dl increased from baseline to day 28 with both empagliflozin doses, without increasing time spent with hypoglycemia.[19]

In another randomized, double-blind trial, newly diagnosed Chinese T2DM patients with HbA1c levels of 7.5%–10.5% were treated with dapagliflozin 5 mg or 10 mg once-daily or placebo. Dapagliflozin treatment for 24 weeks resulted in significant improvement in the mean amplitude of glycemic excursion, reduction in 24-h mean blood glucose, and lower mean plasma glucose concentrations.[20] In another randomized, double-blind study, dapagliflozin 10 mg/day was compared with placebo in adult patients with uncontrolled T2DM on either stable doses of metformin monotherapy (≥1500 mg/day) or insulin (≥30 U/day with or without up to two OADs). Data indicated a notable downward shift in the mean 24-h CGM glucose profile across the overall 24-h profile from baseline to week 4 in the dapagliflozin group, with an improvement in MAGE and glycemic parameters.[21]

Results from the above studies demonstrate SGLT2 inhibitors to be a useful treatment option in T2DM patients with an increased risk of hypoglycemia. The findings also indicate that SGLT2 inhibitors may be considered as an alternative therapeutic option to DPP4 inhibitors in the management of glycemic variability in T2DM patients. Furthermore, the common adverse effects reported with other oral hypoglycemic agents, such as weight gain and hypoglycemia, are not often reported with SGLT2 inhibitors. Therefore, in this patient, treatment with sulfonylurea was discontinued, and therapy with SGLT2 inhibitor was initiated. The SGLT2 inhibitor was selected over a DPP4 inhibitor based on the 2019 American Diabetes Association guidelines and 2019 ESC Clinical Practice Guidelines

Diabetes - in collaboration with the European Association for the Study of Diabetes (EASD), which recommend an SGLT2 inhibitor as a choice of antidiabetic therapy in cases of T2DM with multiple cardiovascular risk factors, and T2DM with an established atherosclerotic CVD. Since the patient was obese and had a family history of CVD, an SGLT2 inhibitor was recommended in this case.[22,23]

Thus, CGM is an effective aid to understand the blood glucose fluctuations caused by diet, lifestyle and treatment, thereby instilling healthy lifestyle choices. The use of CGM is expected to help increase compliance and promote more effective communication between patients and physicians. This case report also highlights the need to emphasize the importance of dietary recommendations for the effective management of hypoglycemia.

CONCLUSION

Glycemic variability poses a major challenge in the management of diabetes. The patients with glycemic variability might present with the disparity between FPG and PPG and HbA1c levels. AGP will facilitate in identifying such cases more accurately, conjointly aiding in framing appropriate management strategies. Careful evaluation and appropriate management using AGP would prevent complications in such patients and improve clinical outcomes. Further, SGLT2 inhibitors were effective in addressing glycemic variability without triggering hypoglycemic risk.

ACKNOWLEDGEMENTS

Author would like to thank Abbott Healthcare Pvt Ltd for providing editorial support for this manuscript.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Little M, Humphries S, Patel K, Dewey C. Decoding the type 2 diabetes epidemic in rural India. Med Anthropol. 2017 Feb 17;36(2):96-110.
2. Unnikrishnan R, Anjana RM, Deepa M, Pradeepa R, Joshi SR, Bhansali A, et al. Glycemic control among individuals with self-reported diabetes in India-the ICMR-INDIAB study. Diabe Technol Therap. 2014 Sep 1;16(9):596-603.
3. Forum GP. Glycemic Pentad. J Assoc Phys Ind. 2017 Jul;65(7):68-79.
4. Bergenstal RM. Glycemic variability and diabetes complications: does it matter? Simply put, there are better glycemic markers!. Diabe Care. 2015 Aug 1;38(8):1615-21.
5. Brownlee M. Biochemistry and molecular cell biology of diabetic complications. Nature. 2001 Dec;414(6865):813.
6. Monnier L, Mas E, Ginet C, Michel F, Villon L, Cristol JP, et al. Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes. Jama. 2006 Apr 12;295(14):1681-7.
7. Gimeno-Orna JA, Castro-Alonso FJ, Boned-Juliani B, Lou-Arnal LM. Fasting plasma glucose variability as a risk factor of retinopathy in type 2 diabetic patients. J Diabe Complicat. 2003 Mar 1;17(2):78-81.
8. Hsu CR, Chen YT, Sheu WH. Glycemic variability and diabetes retinopathy: a missing link. J Diabe Complicat. 2015 Mar 1;29(2):302-6.
9. Zoppini G, Verlato G, Targher G, Casati S, Gusson E, Biasi V, et al. Is fasting glucose variability a risk factor for retinopathy in people with type 2 diabetes?. Nutrit, Metab Cardiovas Dis. 2009 Jun 1;19(5):334-9.
10. Bragd J, Adamson U, Bäcklund LB, Lins PE, Moberg E, Oskarsson P. Can glycaemic variability, as calculated from blood glucose self-monitoring, predict the development of complications in type 1 diabetes over a decade?. Diab Metab. 2008 Dec 1;34(6):612-6.
11. Oyibo SO, Prasad YD, Jackson NJ, Jude EB, Boulton AJ. The relationship between blood glucose excursions and painful diabetic peripheral neuropathy: a pilot study. Diab Med. 2002 Oct;19(10):870-3.
12. Jin SM, Kim TH, Oh S, Baek J, Joung JY, Park SM, et al. Association between the extent of urinary albumin excretion and glycaemic variability indices measured by continuous glucose monitoring. Diab Med. 2015 Feb;32(2):274-9.
13. Muggeo M, Verlato G, Bonora E, Zoppini G, Corbellini M, De Marco R. Long-term instability of fasting plasma glucose, a novel predictor of cardiovascular mortality in elderly patients with non–insulin-dependent diabetes mellitus: the Verona Diabetes Study. Circulation. 1997 Sep 16;96(6):1750-4.
14. Smith-Palmer J, Brändle M, Trevisan R, Federici MO, Liabat S, Valentine W. Assessment of the association between glycemic variability and diabetes-related complications in type 1 and type 2 diabetes. Diab Res Clin Pract. 2014 Sep 1;105(3):273-84.
15. Monnier L, Colette C, Owens DR. The application of simple metrics in the assessment of glycaemic variability. Diabe Metab. 2018 Sep 1;44(4):313-9.
16. Nalysnyk L, Hernandez-Medina M, Krishnarajah G. Glycaemic variability and complications in patients with diabetes mellitus: evidence from a systematic review of the literature. Diabe, Obes Metab. 2010 Apr;12(4):288-98.
17. Krhač M, Lovrenčić MV. Update on biomarkers of glycemic control. World J Diab. 2019 Jan 15;10(1):1.
18. Chilelli NC, Burlina S, Sartore G, Lapolla A. Between reduction of glucose fluctuations and

increased therapeutic adherence: an example of the benefits of vildagliptin in an elderly diabetic patient. Aging Clin Exper Res. 2015 Feb 1;27(1):85-7.
19. Nishimura R, Tanaka Y, Koiwai K, Inoue K, Hach T, Salsali A, et al. Effect of empagliflozin monotherapy on postprandial glucose and 24-hour glucose variability in Japanese patients with type 2 diabetes mellitus: a randomized, double-blind, placebo-controlled, 4-week study. Cardio Diabetol. 2015 Dec;14(1):11.
20. Li FF, Gao G, Li Q, Zhu HH, Su XF, Wu JD, et al. Influence of dapagliflozin on glycemic variations in patients with newly diagnosed type 2 diabetes mellitus. J Diabe Res. 2016;2016.
21. Henry RR, Strange P, Zhou R, Pettus J, Shi L, Zhuplatov SB, et al. Effects of dapagliflozin on 24-hour glycemic control in patients with type 2 diabetes: a randomized controlled trial. Diabe Technol Therap. 2018 Oct 25;20(11):715-24.
22. American Diabetes Association. 7. Diabetes Technology: Standards of Medical Care in Diabetes-2019. Diabe Care. 2019 Jan;42(1):S71-S80.
23. Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, et al. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. Eur Heart J. 2019 Aug 31.

Cite this article as: Saboo B. Role of ambulatory glucose profile in identifying and managing a patient with disparity between FPG, PPG and HbAlc levels: a case report. Int J Res Med Sci 2020;8:738-42.