



DISCORDANCE BETWEEN HbA1c AND FASTING PLASMA GLUCOSE IN REACTIVE HYPOGLYCEMIA: A CASE SERIES

General Medicine

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ABSTRACT

Background: Reactive Hypoglycemia (post prandial hypoglycemia) refers to recurrent episodes of low blood glucose levels that occur hours after a meal – usually within 2-5 hours after eating. It is considered to be a prediabetic state. **Aims and Objectives:** We looked at the data of 15 patients diagnosed with reactive hypoglycemia based on the evidence of Continuous Glucose Monitoring, to determine the correlation of reactive hypoglycemia with HbA1c and Fasting Plasma Glucose. **Results:** In this series we observed a discordance between HbA1c and Fasting Plasma Glucose in patients with Reactive Hypoglycemia. In addition, there was also a subset of patients that demonstrated normal HbA1c and Fasting Plasma Glucose. **Conclusion:** As it has been observed that patients with suspected Reactive Hypoglycemia show varied discordance between HbA1c and Fasting Plasma Glucose, it is recommended to use Continuous Glucose Monitoring in the evaluation of all patients with a suspicion of Reactive Hypoglycemia

KEYWORDS

Reactive Hypoglycemia, Continuous Glucose Monitoring, HbA1c, Fasting Plasma Glucose, Prediabetes

INTRODUCTION

Reactive hypoglycemia (RH) is a condition where a person experiences low blood glucose levels (hypoglycemia) within 2-5 hours of eating a meal¹. The clinical features of reactive hypoglycemia include sympathetic signs like anxiety, palpitations, irritability, tremors and sweating, and neuroglycopenic features like hunger, dizziness, tingling, blurred vision, difficulty thinking and faintness². Although reactive hypoglycemia is known to occur in patients with or without diabetes, it is considered to be a prediabetic state³.

Glycated hemoglobin (HbA1c), a blood test that measures a person's average blood glucose level over the past two to three months is one of the recommended tests used to monitor blood glucose control in people with diabetes along with fasting plasma glucose (FPG)⁴. However, HbA1c has its limitations in giving a complete picture of glycemic control over the previous two to three-month period. A normal HbA1c level does not necessarily mean a consistently controlled blood glucose level. Firstly, since the HbA1c is a single average value, it may mask wide fluctuations due to episodes of hyperglycemia and hypoglycemia in the same patient. Secondly, HbA1c can only give the average and it cannot pinpoint the actual timings of hypoglycemia. Thirdly, HbA1c exhibits individual differences where some people may have high risk of hypoglycemia even when their HbA1c is in the normal range.

Different methods have been employed to detect RH in clinical practice. These include Oral Glucose Tolerance Test (OGTT), periodic ambulatory blood glucose testing and Continuous Glucose Monitoring (CGM). Of these CGM is the most sensitive and specific in detecting episodes of RH⁵. CGM measures the glucose level in the interstitial fluid by means of a sensor that is attached to the body and automatically records frequent glucose readings⁶. These readings are then transferred either manually or wirelessly to a device that can display the patient's glucose levels over time (Figure 1).

The exact mechanism of Reactive Hypoglycemia is not known. But it is believed that it may due to (a) an exaggerated insulin response, either related to insulin resistance or an increased glucagon-like-peptide 1 (b) defects in glucagon response; (c) high insulin sensitivity⁷.

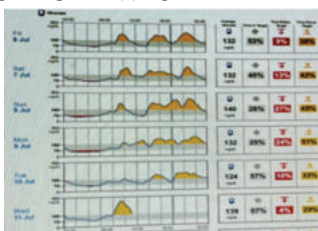


Figure 1: CGM Recording Of Patient: Yellow Peaks Represent

Episodes Of Hyperglycemia While Red Troughs Represent Hypoglycemic Episodes.

AIMS AND OBJECTIVES OF THE STUDY

The aim of this study was to describe the discordance between HbA1c and FPG in RH patients in terms of the following:

- Patients with normal HbA1c and high FPG
- Patients with normal HbA1c and normal FPG
- Patients with high HbA1c and high FPG

METHODOLOGY

Reactive Hypoglycemia (RH) was diagnosed by means of Continuous Glucose Monitoring (CGM) done over a period of 14 days in all patients. Fasting Glucose and HbA1c level were also estimated in all patients in the series.

RESULTS AND DISCUSSION

In this study conducted at a multispecialty hospital, a total of 15 reactive hypoglycemic cases, with diagnosis confirmed by CGM were taken from the General Medicine Department to assess the discordance between HbA1c and FPG.

TABLE 1: HbA1c and FPG levels in the series. Green – nondiabetic; Yellow – Prediabetic; Red – discordance of HbA1c and FPG; Blue – Diabetes

SL NO	HbA1c (%)	FPG (mg/dl)
1.	6	100
2.	5.2	92
3.	5.4	100
4.	6.4	126
5.	5.6	100
6.	4.7	94
7.	5.5	99
8.	6.9	125
9.	5.4	112
10.	6.5	128
11.	5.8	115
12.	6.7	133
13.	6.5	124
14.	5.9	118
15.	5.8	103

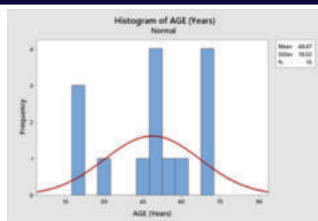


Figure 2: Distribution Of Age

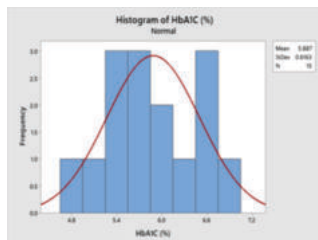


Figure 3: Distribution Of Hba1c

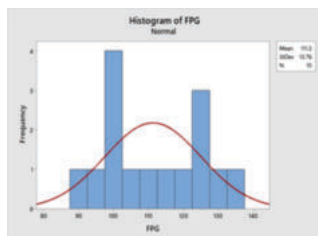


Figure 4: Distribution Of Fpg

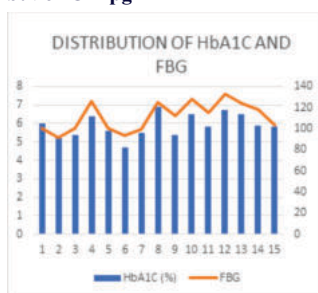


Figure 5: Comparative Distribution Of Hba1c And Fpg

The objective of the study was to determine the discordance between HbA1c and FPG. 15 samples from the general medical department make up the study population (Table 1). CGM was used to examine each of these patients to confirm the occurrence of RH. Non-diabetic people are those with HbA1c < 5.7 and FPG values under 99. While an HbA1c between 5.7 – 6.4 % and an FPG reading of 100 – 125mg/dl is regarded as pre-diabetic, and anything more than that indicates diabetes mellitus⁴.

Among the 15 data collected, from age 18 to 71, the mean value of age is 48.67 years with standard deviation 18.52 (Figure 2). Normal HbA1c (<5.7) were found in 6 patients (40%), with mean value of 5.8 and standard deviation of 0.616. Normal FPG levels were found in 3 patients (20%) with mean value of 111.3 and standard deviation of 13.76.

Reactive Hypoglycemia with normal HbA1c value and High FPG value was seen in 3 patients (20%). This finding was similar to the case report published by Veerasak Sarinnapakorn, et al, which concluded that the patient with reactive hypoglycemia had normal HbA1c levels but high fasting blood sugar levels⁵. In our study we also observed that RH was seen in 3 patients (20%) with normal HbA1c and normal FPG values. This is similar to a retrospective study conducted by Tanushree Jain, where they found that reactive hypoglycemia can occur in individuals with normal HbA1c levels and normal fasting blood glucose levels⁸.

CONCLUSION

Features of Reactive hypoglycemia differ from person to person, depending on different physiological factors. From this study we

observed that Reactive hypoglycemia can be found in persons with normal HbA1c and high FPG values, also with normal HbA1c and normal FPG level. Low HbA1c and normal FPG values were not seen as predictors of RH. Our study clearly showed that there is a discordance between HbA1c and FPG in RH. Hence CGM is the tool which can help in specifically identifying RH in patients with normal HbA1c and FPG, and also abnormal HbA1c and FPG. Therefore, CGM has a great role in diagnosing RH beyond our conventional tools.

List Of Abbreviations

CGM: Continuous Glucose Monitoring

FPG: Fasting Plasma Glucose

HbA1c: Glycated Hemoglobin

RH: Reactive Hypoglycemia

REFERENCES

- Altuntaş Y. Postprandial Reactive Hypoglycemia. Sisli Etfal Hastan Tip Bul. 2019 Aug 28;53(3):215-220. doi:10.14744/SEMB.2019.59455.
- Brun JF, Fedou C, Mercier J. Postprandial reactive hypoglycemia. Diabetes Metab. 2000;26(5):337-351.
- Ly X, Fang K, Hao W, et al. Identification of Reactive Hypoglycemia with Different Basic BMI and Its Causes by Prolonged Oral Glucose Tolerance Test. Diabetes Metab Syndr Obes. 2020 Dec 2;13:4717-4726. doi: 10.2147/DMSO.S280084. PMID: 33293845; PMCID: PMC7719337.
- Nuha A, ElSayed, Grazia Aleppo, Vanita R. Aroda, et al. Classification and Diagnosis of Diabetes: Standards of Care in Diabetes—2023. Diabetes Care 1 January 2023; 46 (Supplement 1)
- Petrie JR, Peters AL, Bergenstal RM, et al. Improving the clinical value and utility of CGM systems: issues and recommendations: a joint statement of the European Association for the Study of Diabetes and the American Diabetes Association Diabetes Technology Working Group [published online October 25, 2017] Diabetologia. 2017;60(12):2319–2328. doi: 10.1007/s00125-017-4463-4.
- Funtanilla VD, Candidate P, Caliendo T, Hilar O. Continuous Glucose Monitoring: A Review of Available Systems. PT. 2019 Sep;44(9):550-553. PMID: 31485150; PMCID: PMC6705487.
- Veerasak Sarinnapakorn, et al; Discordance between fasting plasma glucose and HbA1c in the diagnosis and management of diabetes, doi:10.30574/wjarr.2021.12.1.0521.
- Tanushree Jain, Reactive Hypoglycemia of Pre-diabetics “ A diagnostic Delima”; 2019 January; doi:2395.311X.5219.10.