

Comparative analysis of fructosamine and HbA1c as a glycemic control marker in Type 2 diabetes patients in a tertiary care hospital study



Harshvardhan Patel¹, Anuradha N²

¹Junior Resident, ²Associate Professor, Department of General Medicine, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India

Submission: 06-04-2022

Revision: 02-09-2023

Publication: 01-10-2023

ABSTRACT

Background: Fructosamine (FA) is a marker of plasma glucose value that reveals the short-term glycemic level for 2–3 weeks. While measuring the plasma glucose level over 2–3 months with glycated hemoglobin (HbA1c) is a common practice. **Aims and Objectives:** This study aims to demonstrate the relationship between HbA1c and FA levels in Type II diabetes mellitus. **Materials and Methods:** This prospective and cross-sectional study was conducted from January 2021 to January 2022, involving Type 2 diabetic patients attending both inpatient and outpatient at Sree Balaji Medical College and Hospital, Chennai. HbA1C, FA, postprandial blood sugar (PPBS), and fasting blood sugar (FBS) were estimated. The collected data were analyzed with IBM SPSS Statistics for Windows, Version 23.0. (Armonk, NY: IBM Corp). To assess the relationship between the variables, Pearson's Correlation was used. **Results:** We analyzed 61 known Type 2 diabetic subjects in our study. Most patients were in the 51–60 age groups, with the mean age of the cohorts being 56.2 years, SD ± 10.1. There were 28 females and 33 in this study. Comparing HbA1c with FA, a statistically significant correlation was noted ($P < 0.001$), with a Pearson correlation value of 0.924. A similar strong positive correlation was also noted between HbA1c and FBS, PPBS, and FA, and PPBS. **Conclusion:** The link between FA and HbA1c is highlighted in this study. Since FA's correlation with HbA1c is proven to be statistically significant, it can be utilized as an alternative to or addition to HbA1c in the assessment of blood glucose management.

Key words: Glycosylated hemoglobin; Fructosamine; Type II diabetes mellitus

INTRODUCTION

Diabetes has become one of the most dangerous and prevalent chronic diseases of our day, lowering life expectancy and creating life-threatening, disabling, and expensive complications. The ninth edition of the International Diabetes Federation reported a prevalence of 9% (463 million adults) in 2019, indicating that the global prevalence of diabetes had reached pandemic levels. By 2030, it will reach 10.2% (578 million), and by 2045, 10.9% (700 million). Urban areas (10.8%) and high-income countries (10.4%) have greater prevalence rates than rural

areas (7.2%) and low-income countries (4.0%), respectively. One in two (50.1%) people with diabetes is unaware that they have the disease. Impairment in glucose tolerance is predicted to affect 7.5% (374 million) people worldwide in 2019 and 8.0% (454 million) people by 2030, and 8.6% (548 million) people by 2045.^{1,2}

Diabetes has been classified as Type 1 diabetes; Type 2 diabetes; gestational diabetes; and diabetes with a particular etiology that may be genetic (monogenic types such as maturity-onset diabetes in young people) or secondary to medicines, pancreatic factors, or other disorders. Type 1 and

Access this article online

Website:

<http://nepjol.info/index.php/AJMS>

DOI: 10.3126/ajms.v14i10.53962

E-ISSN: 2091-0576

P-ISSN: 2467-9100

Copyright (c) 2022 Asian Journal of Medical Sciences



This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

Address for Correspondence:

Dr. Anuradha N, Associate Professor, Department of General Medicine, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India. **Mobile:** +91-9841424677. **E-mail:** anu_madras@yahoo.com

Type 2 combined make up the primary burden of diabetes is diabetes.³ The interplay of genetic, environmental, and other risk factors primarily causes Type 2 diabetes mellitus (T2DM). T2DM also develops more quickly when the first phase of insulin release is lost, basal insulin secretion is abnormally pulsatile, and glucagon production is enhanced. Although T2DM patients often do not require exogenous insulin, they might if blood glucose levels are not adequately managed by diet or oral hypoglycemic medications. In addition, problems, including cardiovascular conditions, diabetic neuropathy, nephropathy, and retinopathy, are frequently present in T2DM patients.⁴

The gold standard for monitoring glucose levels in diabetic patients is now glycated hemoglobin (HbA1c). However, factors that affect changes in hemoglobin metabolism can affect HbA1c tests' accuracy. Alternative glycemia indicators, such as fructosamine (FA), have been shown to supplement HbA1c or serve as a reliable substitute for HbA1c. In addition, FA represents exposure shorter than HbA1c, which may be useful for monitoring fast metabolic changes or changes in diabetes treatment.⁵

Aims and objectives

This study aimed to compare and analyze FA and HbA1c in Type 2 diabetes patients as glycemic control markers.

MATERIALS AND METHODS

This prospective and cross-sectional study was conducted from January 2021 to January 2022, involving Type 2 diabetic patients attending both inpatient and outpatient at Sree Balaji Medical College and Hospital, Chennai. After the ethical committee's approval, informed consent was obtained from the patients before initiation of the study.

Inclusion criteria

Participants with T2DM, age 18 years or older, treatment with oral hypoglycemic agents or insulin, ability to provide informed consent, and compliance with study procedures were included in the study.

Exclusion criteria

Type 1 diabetic persons, prediabetics, critically ill patients, and those under 35 years and older than 80 were excluded from the study.

Exclusion criteria might include pregnant or lactating women, those with end-stage renal disease, severe liver disease, or any other condition that might interfere with the interpretation of the results.

Demographic data of patients were collected. Fasting blood sugar (FBS), postprandial blood sugar (PPBS), FA, and

HbA1c were measured in all 61 patients after obtaining informed consent. Roche Cobas C311 measured FA, and HbA1c was measured with a Bio-Rad D-10 machine and evaluated with the principle based on HPLC.

The collected data were analyzed with IBM SPSS Statistics for Windows, Version 23.0. (Armonk, NY: IBM Corp). Percentage analysis was used for categorical variables, and the mean and SD were used for continuous variables to describe the data descriptive statistics frequency analysis. To assess the relationship between the variables, Pearson's correlation was used. Categorical data, such as age group, gender, BMI, FBS, PPBS, HbA1c, and FA, were presented as numbers and percentages. The Mean and Standard deviation of FBS, PPBS HbA1c, and FA were also calculated, and the probability value of 0.05 is considered significant.

RESULTS

We analyzed 61 known Type 2 diabetic subjects in our study. The cohort's ages ranged from 36 to 77 years (mean 56.2, SD±10.1). Table 1 gives the age-wise distribution of study subjects. Most of the patients were in the 51–60 age groups. There were 28 (45.9%) females and 33 (54.1%) in this study.

On assessing the BMI, it was noted that 21 subjects had BMI <25, 25 had BMI between 25 and 29, and 15 had BMI ≥30. FBS levels showed that 10 (16.4%) had FBS values <126, while 52 (83.6%) had HbA1c analysis showed 05 subjects had levels <6.5, and 56 had HbA1c ≥6.5. In 11.5% (n=07) patients, FA was ≤285, and in 88.5% (n=54), it was >285. The clinical characteristics of all the subjects are presented in Table 2.

Table 3 shows the comparative analysis of HbA1c, FA, FBs, and PPBS. Comparing HbA1c with FA, a statistically significant correlation was noted (P<0.001), with a Pearson correlation value of 0.924. Graph 1 shows the relationship of HbA1c with FA. HbA1c, when compared to FBS, a statistically significant correlation was noted (P<0.001), with a Pearson correlation value of 0.894. The scatter plot in Graph 2 represents the relationship between HbA1c and FBS. Comparing HbA1c with PPBS showed a statistically significant correlation (P<0.001), with a Pearson correlation

Table 1: Age-wise distribution of study subjects

Age	Frequency	Percent
≤40 years	1	1.6
41–50 years	18	29.5
51–60 years	25	41.0
>60 years	17	27.9
Total	61	100.0

Table 2: Clinical characteristics of all the subjects

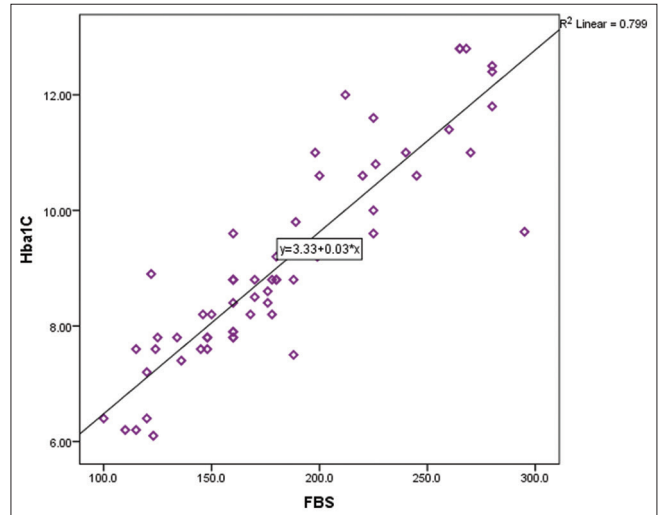
Parameters	n	Minimum	Maximum	Mean	SD
Age	61	36	77	56.2	10.1
BMI	61	19	34	26.7	4.0
HbA1C	61	6.10	12.80	9.1	1.8
Fructosamine	61	260	440	341.3	49
FBS	61	100	295	182.9	50.6
PPBS	61	140	386	242.5	68.9

FBS: Fasting blood sugar, PPBS: Postprandial blood sugar, BMI: Body mass index, HbA1C: Glycated hemoglobin

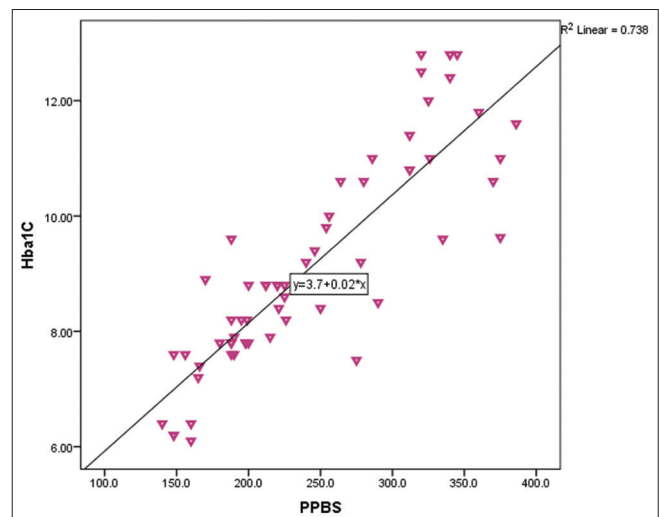
Table 3: Comparative analysis of HbA1c, Fructosamine, FBS, and PPBS

Parameters	Fructosamine	FBS	PPBS
HbA1C			
r-value	0.924	0.894	0.859
P-value	<0.001	<0.001	<0.001
n	61	61	61
Fructosamine			
r-value	1	0.849	0.822
P-value		<0.001	<0.001
n	61	61	61
FBS			
r-value		1	0.933
P-value			<0.001
n	61	61	61

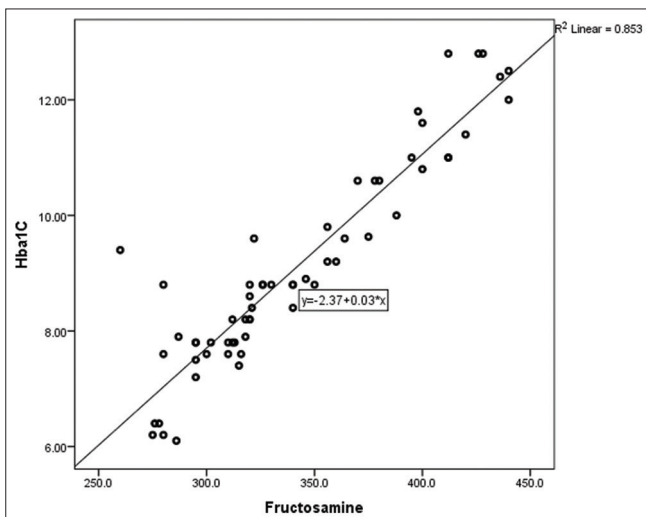
FBS: Fasting blood sugar, PPBS: Postprandial blood sugar, BMI: Body mass index, HbA1C: Glycated hemoglobin



Graph 2: Scatter plot of glycated hemoglobin compared with fasting blood sugar



Graph 3: Scatter plot of glycated hemoglobin compared with postprandial blood sugar



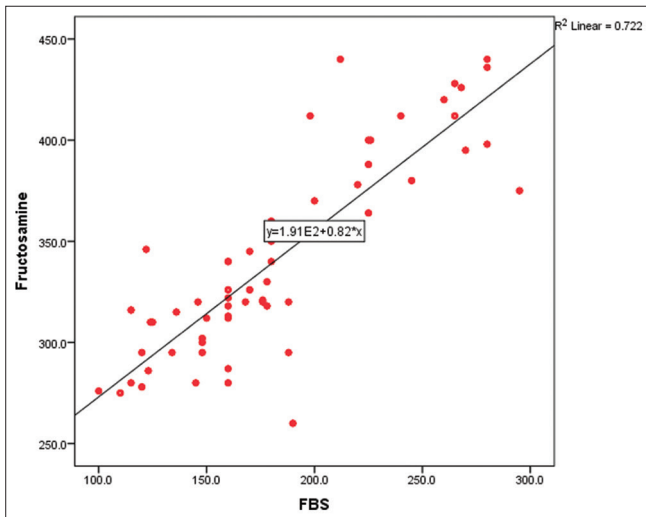
Graph 1: Scatter plot of glycated hemoglobin compared with fructosamine

value of 0.859. The relationship between HbA1c and PPBS is depicted in the scatter plot in Graph 3; when FA was compared with FBS and PPBS, a statistically significant observation was found ($P < 0.001$), with a significant Pearson correlation value of 0.849 and 0.822, respectively (Graphs 4 and 5). FBS and PPBS comparison also showed a strong statistical significance ($P < 0.001$, $r = 0.933$). The comparative values are represented in Graph 6.

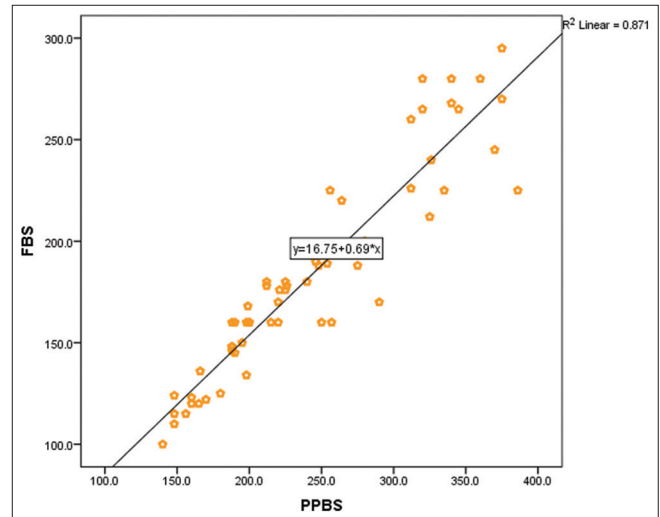
DISCUSSION

The 61 patients who visited the inpatient and outpatient of Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, provided the data for our study. Our study found a significant correlation ($P < 0.001$) between HbA1C, FA, FBS and FA, and FBS and PPBS. Numerous other investigations have also defined a strong association between these markers and a similar outcome.

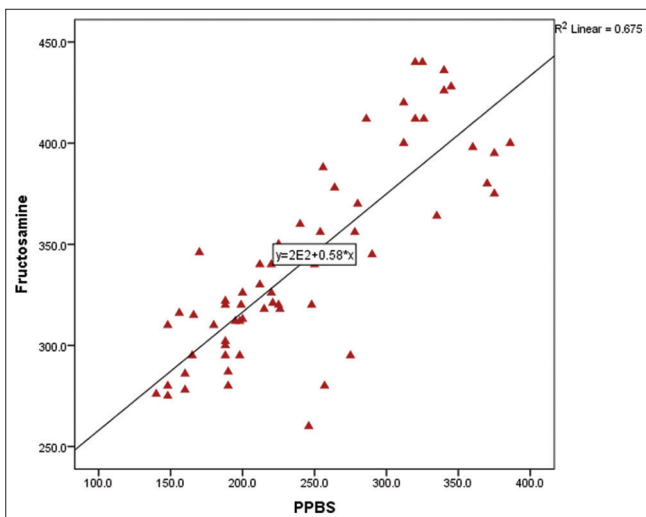
The most popular biomarker for detecting diabetes and prediabetes is HbA1c. When glucose binds to the aminoterminal group of the hemoglobin subunit, HbA1c is created. HbA1c rather than glucose levels at a single time point reflects chronic glycemia. Increased morbidity and death are linked to higher HbA1c values.^{6,7} Compared



Graph 4: Scatter plot of fructosamine compared with fasting blood sugar



Graph 6: Scatter plot of fasting blood sugar compared with postprandial blood sugar



Graph 5: Scatter plot of fructosamine compared with postprandial blood sugar

to fasting plasma glucose and the oral glucose tolerance test, HbA1c provides several benefits, including more convenience due to the lack of a fasting requirement, greater preanalytical stability, and less day-to-day disruption due to stress and illness. HbA1c levels will therefore be impacted by changes in the red blood cell formation rate or circulatory life duration.^{8,9} Iron deficiency anemia, asplenia, folate and Vitamin B12 insufficiency, severe hypertriglyceridemia, and uremia are among the illnesses that can cause HbA1c to be artificially raised. Hemolytic anemia, blood loss, splenomegaly, and end-stage renal failure are all associated with falsely low HbA1c levels. Depending on the method employed, hemoglobin variations such as HbS, HbC, HbD, and HbE may also cause an overestimation or underestimating of HbA1c. For these reasons, a prediabetes diagnosis based solely on

HbA1c may not be sufficient, and a more precise diagnosis may require confirmation using additional biomarkers.⁹⁻¹³

FA also has been employed as a substitute glycemic marker to diagnose diabetes and prediabetes. It can be a helpful clinical marker of short-term glycemic fluctuation and glucose control because it reflects the average blood glucose concentrations over the previous 1–4 weeks. It is beneficial in circumstances that impair hemoglobin reliability. FA may also be a sign of the possibility of microvascular problems. FA may therefore be a useful supplementary marker in clinical situations when HbA1c may not be reliable.^{7,14,15}

A comparable study by Baker et al., found a substantial association between FA and HbA1, and FBS. The researchers found that FA is a quick and easy test that can be utilized as a substitute for the HbA1c marker in evaluating the glycemic index.¹⁶

Goyal et al., aimed to compare FA levels with HbA1c in glycemic control evaluation in Type 2 diabetics to determine the usefulness of FA as an alternative marker for glucose control evaluation. Retrospective data from 48 Type 2 diabetic individuals were collected for this cross-sectional investigation. Akin to our study, the analysis of glycemic control showed that FA and HbA1C levels have a statistically significant correlation with each other ($P < 0.001$).¹⁷

A study by Koskinen et al., discovered a strong association between FA and others with FBS, mean blood sugar, and HbA1c values. In addition, this study indicated FA is convenient and affordable and may be utilized to evaluate glycemic control.¹⁸

A prospective, single-center, and observational study by Stylin et al., aimed to compare and correlate the efficacy of HbA1c and FA levels in diagnosing T2DM. In this study, 90 people with Type II diabetes were included. In this research group, both sexes are represented. Study participants include those between 30 and 60 with HbA1c levels of more than 6.5%. This study showed a weak positive correlation between HbA1c and FA value ($r=0.23$, $P=0.02$), which is statistically significant. In comparison, our study showed a statistically significantly positive, strong correlation ($r=0.933$, $P<0.001$).¹⁹

In the 1990–1992 community-based atherosclerosis risk in communities study, 11,104 people with and without diabetes underwent glycated albumin and FA measurements. Similar to the present study, Pearson's correlations of HbA1c with FA were high ($r=0.81$) in the overall population but lower when the cohorts were limited to persons without diabetes. Their findings concluded that FA could be helpful when HbA1c testing is impossible, or its interpretation presents challenges.

Contrary to the present study, where FBS found a significant positive correlation with FA and HbA1c, the study by Lim et al., found that FBS has little predictive value for glycemic control levels compared to FA, especially in patients with well-controlled diabetes.²⁰

Some studies have found contrary findings. Shima et al., used HbA1c, FA, and glycated albumin to screen for diabetes in 302 adults. They concluded that the plasma levels of glycated albumin and HbA1c, but not FA, could efficiently identify subjects at risk of diabetes.²¹

In a prospective, randomized, multicenter, and controlled research with 72 diabetic patients, Lindsey et al., evaluated the relationship between FA and HbA1c. They found that the amalgamation of weekly FA testing and daily blood glucose monitoring was not superior to the regular monitoring of glucose alone.²² Joy et al., in a study of 23 diabetic hemodialysis patients, showed that FA was not significantly associated with long-term glycemic control in diabetic patients on hemodialysis ($r=0.345$, $P=0.11$).²³

Early diabetes diagnosis and strict glucose management are essential for stopping or delaying the onset of significant, perhaps fatal, and complications. Although HbA1c is still the gold standard for diagnosing diabetes and glycemic control, new research shows that other biomarkers, such as FA and GA, are replacing HbA1c in some patients when the measurement of HbA1c may be inaccurate or even biased. This particularly applies to patients with CKD, red blood cell abnormalities, fast changes in glucose homeostasis, and higher glycemic excursions (i.e., transiently high blood

glucose rises). Our results add to the growing body of research suggesting that FA or glycated albumin may be helpful in cases where HbA1c testing is not feasible or when its interpretation is difficult.

Limitations of the study

A modest sample size was used for this investigation. A bigger sample size and comparison with the non-diabetic population would have been beneficial to obtain more information.

CONCLUSION

The present study found that HbA1c correlated significantly with FA ($r=0.924$, $P=0.001$). Further, we also noted a statistically strong correlation between FA with FBS and PPBS. Newer markers like FA can help evaluate short-term blood sugar variations. It can also complement HbA1c or be used as a stand-alone glycemic index marker in certain situations. The findings of this study suggest that in the diagnosis and management of diabetes patients, it will be scientific and logical if HbA1c and FA are measured jointly. Although FA is not frequently used in clinical practice, it can be a helpful marker for other purposes besides glycemic control evaluation.

ACKNOWLEDGMENT

We want to express our sincere gratitude to the patients who took part in this study. Their contribution was invaluable in generating the data and insights presented in this research paper. We also extend our appreciation to the head of the department, as well as the medical staff, for their support and dedication throughout the study.

REFERENCES

1. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract.* 2022;183:109119. <https://doi.org/10.1016/j.diabres.2021.109119>
2. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract.* 2019;157:107843. <https://doi.org/10.1016/j.diabres.2019.107843>
3. American Diabetes Association Professional Practice Committee. 2. Classification and diagnosis of diabetes: Standards of medical care in diabetes-2022. *Diabetes Care.* 2022;45(Suppl 1):S17-S38. <https://doi.org/10.2337/dc22-S002>
4. Wu Y, Ding Y, Tanaka Y and Zhang W. Risk factors contributing to Type 2 diabetes and recent advances in the treatment and

- prevention. *Int J Med Sci.* 2014;11(11):1185-1200.
<https://doi.org/10.7150/ijms.10001>
5. Ribeiro RT, Macedo MP and Raposo JF. HbA1c, fructosamine, and glycated albumin in the detection of dysglycaemic conditions. *Curr Diabetes Rev.* 2016;12(1):14-19.
<https://doi.org/10.2174/1573399811666150701143112>
 6. Bookchin RM and Gallop PM. Structure of hemoglobin A1c: Nature of the N-terminal beta chain blocking group. *Biochem Biophys Res Commun.* 1968;32(1):86-93.
[https://doi.org/10.1016/0006-291x\(68\)90430-0](https://doi.org/10.1016/0006-291x(68)90430-0)
 7. Dorcely B, Katz K, Jagannathan R, Chiang SS, Oluwadare B, Goldberg IJ, et al. Novel biomarkers for prediabetes, diabetes, and associated complications. *Diabetes Metab Syndr Obes.* 2017;10:345-361.
<https://doi.org/10.2147/DMSO.S100074>
 8. Sacks DB, Brunz DE, Goldstein DE, Maclaren NK, McDonald JM and Parrott M. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Clin Chem.* 2002;48(3):436-472.
<https://doi.org/10.1093/clinchem/48.3.436>
 9. Radin MS. Pitfalls in hemoglobin A1c measurement: When results may be misleading. *J Gen Intern Med.* 2014;29(2):388-394.
<https://doi.org/10.1007/s11606-013-2595-x>
 10. Lee JE. Alternative biomarkers for assessing glycemic control in diabetes: Fructosamine, glycated albumin, and 1,5-anhydroglucitol. *Ann Pediatr Endocrinol Metab.* 2015;20(2):74-78.
<https://doi.org/10.6065/apem.2015.20.2.74>
 11. Malmström H, Walldius G, Grill V, Jungner I, Gudbjörnsdóttir S and Hammar N. Fructosamine is a useful indicator of hyperglycaemia and glucose control in clinical and epidemiological studies--cross-sectional and longitudinal experience from the AMORIS cohort. *PLoS One.* 2014;9(10):e111463.
<https://doi.org/10.1371/journal.pone.0111463>
 12. Bry L, Chen PC and Sacks DB. Effects of hemoglobin variants and chemically modified derivatives on assays for glycohemoglobin. *Clin Chem.* 2001;47(2):153-163.
<https://doi.org/10.1093/clinchem/47.2.153>
 13. Sacks DB, Arnold M, Bakris GL, Brunz DE, Horvath AR, Kirkman MS, et al. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Clin Chem.* 2011;57(6):e1-e47.
<https://doi.org/10.1373/clinchem.2010.161596>
 14. Schleicher ED, Olgemöller B, Wiedenmann E and Gerbitz KD. Specific glycation of albumin depends on its half-life. *Clin Chem.* 1993;39(4):625-628.
<https://doi.org/10.1093/clinchem/39.4.625>
 15. Selvin E, Francis LM, Ballantyne CM, Hoogeveen RC, Coresh J, Brancati FL, et al. Nontraditional markers of glycemia: Associations with microvascular conditions. *Diabetes Care.* 2011;34(4):960-967.
<https://doi.org/10.2337/dc10-1945>
 16. Baker JR, Metcalf PA, Johnson RN, Newman D and Rietz P. Use of protein-based standards in automated colorimetric determinations of fructosamine in serum. *Clin Chem.* 1985;31(9):1550-1554.
<https://doi.org/10.1093/clinchem/31.9.1550>
 17. Goyal J, Das N, Kumar N, Raghav M, Bhatia PS, Singh KP, et al. Comparative evaluation of fructosamine and HbA1c as a marker of glycemic control in Type 2 diabetes: A hospital based study. *Int J Health Sci Res.* 2019;9(9):269-274.
 18. Koskinen P, Irjala K, Viikari J, Panula-Ontto R and Matikainen MT. Serum fructosamine in the assessment of glycaemic control in diabetes mellitus. *Scand J Clin Lab Invest.* 1987;47(3):285-292.
<https://doi.org/10.3109/00365518709168903>
 19. Stylin AG, Pallinti V and Silambanan SS. Correlation of HbA1c and fructosamine in Type II diabetes mellitus. *J Pharm Sci Res.* 2020;12(6):821-824.
 20. Lim TO, Selvan T, Suppiah A, Khan N, Ismail F. Comparison of serum fructosamine and blood glucose concentrations as indices of glycaemic control in non-insulin dependent diabetic out-patients. *Singapore Med J.* 1992;33(3):287-9.
 21. Shima K, Abe F, Chikakiyo H and Ito N. The relative value of glycated albumin, hemoglobin A1c and fructosamine when screening for diabetes mellitus. *Diabetes Res Clin Pract.* 1989;7(4):243-250.
[https://doi.org/10.1016/0168-8227\(89\)90011-9](https://doi.org/10.1016/0168-8227(89)90011-9)
 22. Lindsey CC, Carter AW, Mangum S, Greene D, Richardson A, Brown SJ, et al. A prospective, randomized, multicentered controlled trial to compare the annual glycemic and quality outcomes of patients with diabetes mellitus monitored with weekly fructosamine testing versus usual care. *Diabetes Technol Ther.* 2004;6(3):370-377.
<https://doi.org/10.1089/152091504774198070>
 23. Joy MS, Cefalu WT, Hogan SL and Nachman PH. Long-term glycemic control measurements in diabetic patients receiving hemodialysis. *Am J Kidney Dis.* 2002;39(2):297-307.
<https://doi.org/10.1053/ajkd.2002.30549>

Authors' Contributions:

HP- Manuscript preparation, literature review, data collection, data analysis; AN- Protocol review, and editing manuscript.

Work attributed to:

Department of General Medicine, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India.

Orcid ID:

Dr. Harshvardhan Patel - <https://orcid.org/0000-0001-6322-0463>

Dr. Anuradha N - <https://orcid.org/0000-0002-5784-6483>

Source of Support: Nil, **Conflicts of Interest:** None declared.