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REVIEW ARTICLE

Fructosamine: An Essential Biomarker in the Diabetes Landscape

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ABSTRACT

Diabetes mellitus is a prevalent metabolic disorder that can lead to severe complications if left untreated, largely due to chronic hyperglycemia. Effective diabetes management requires accurate blood glucose monitoring and reliable diagnostic tools. While hemoglobin A1c (HbA1c) is the gold standard for assessing long-term glycemic control, it has limitations, particularly in individuals with conditions affecting red blood cell turnover. Fructosamine offers an alternative, reflecting average blood glucose levels over the previous 2–3 weeks, providing short-term glycemic management insights. This review explores the role of fructosamine in diagnosing and managing diabetes, comparing its effectiveness to the widely used HbA1c test. It focuses on its applicability in specific patient groups, such as those with hemoglobinopathies, chronic kidney disease, and pregnant women. A comprehensive literature review of clinical studies and guidelines was conducted to evaluate fructosamine's diagnostic accuracy, its comparison with HbA1c, and its utility in these special populations. Fructosamine effectively measures glycemic control when HbA1c may be unreliable, offering a cost-effective tool that captures short-term glucose fluctuations. However, its accuracy can be influenced by factors like serum protein levels and inconsistencies in testing methods, indicating a need for further standardization. It concludes that fructosamine is a valuable biomarker for short-term glycemic monitoring, particularly in cases where HbA1c may not provide reliable results. Although it is not yet widely adopted as a primary diagnostic tool, fructosamine holds promise as a complement to HbA1c in the diagnosis and management of diabetes, especially in cases requiring rapid assessment of glycemic changes.

Keywords: Clinical utility, fructosamine, HbA1c in diabetes diagnosis

INTRODUCTION

Insulin production, insulin function, or both deficits are the underlying causes of diabetes mellitus (DM), a complex metabolic condition characterized by consistently high blood sugar levels.[1] By 2021, there will be 537 million diabetics globally, according to the international diabetes federation, and by 2030, that figure is predicted to rise to 643 million. Diabetes is becoming more and more common worldwide, which is concerning.[2] Serious consequences of diabetes, including retinopathy, neuropathy, nephropathy, and cardiovascular disease, are associated with significant morbidity and mortality. Effective care and an accurate diagnosis made early in life are crucial for the well-being of diabetics and for delaying the onset of related complications.[3]

Conventionally, the diagnosis of diabetes has been made using recognized criteria, such as hemoglobin A1c (HbA1c) levels, oral glucose

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tolerance test, and fasting plasma glucose.[4] HbA1c has become well-known among them as a crucial biomarker for identifying and keeping track of long-term glycemic management. The HbA1c test provides important information about a patient's overall metabolic health by reflecting average blood glucose concentrations over the previous 2–3 months.[5] Diabetes is usually diagnosed based on HbA1c readings of 6.5% (48 mmoL/moL) or above, per standards from the World Health Organization (WHO) and the American Diabetes Association.[6]

HbA1c has limits even with its extensive use, especially in some clinical populations. Inaccuracies in HbA1c values can result from illnesses that impact red blood cell turnover, including anemia, hemoglobinopathies (such as sickle cell disease and thalassemia), and chronic renal disease.[7] In these situations, depending on the underlying ailment, HbA1c may either overstate or underestimate typical glucose levels. For instance, because red blood cells have a shorter lifespan in people with high red blood cell turnover, such as hemolytic anemia, HbA1c values may appear deceptively low.[8] In addition, it should be noted that HbA1c is not a reliable indicator of short-term variations in blood glucose levels, which can be important when evaluating the immediate effects of therapeutic interventions, particularly when a patient is pregnant, hospitalized, or undergoing a significant change in their diabetes treatment.[9] Alternative biomarkers for glucose monitoring have been investigated in an effort to overcome these drawbacks. Fructosamine is a marker for glycated serum proteins, mainly albumin, and it indicates the average blood glucose levels throughout the previous 2–3 weeks.[10] In contrast to HbA1c, fructosamine offers a more immediate picture of glycemic control and is not impacted by red blood cell turnover. Due to this feature, it is a useful tool when monitoring quick changes in blood sugar, including when adjusting insulin dosage or implementing dietary modifications.[11] When a patient's HbA1c is unstable, such as when they have hemoglobinopathies, recent blood transfusions, or anemia, fructosamine is especially helpful.[12]

A popular choice in clinical practice, fructosamine testing is easy to use, affordable, and does not need fasting.[13] This is especially true in areas where resources are scarce. The lack of uniformity, variation in testing procedures, and the impact of variables such as serum protein levels on fructosamine concentration have prevented fructosamine from being widely used as a main diagnostic tool for diabetes, despite these benefits.[14] However, studies have demonstrated that fructosamine can supplement HbA1c in some therapeutic circumstances, especially when glycemic surveillance is needed temporarily or when HbA1c readings are not consistent.[15]

In this review, we examine the biochemical makeup of fructosamine, its utility in DM diagnosis and monitoring, as well as its benefits and drawbacks in comparison to HbA1c. We will also look at its clinical uses, especially in populations for which HbA1c may not be able to accurately detect glycemic levels. Finally, we will talk about the latest developments in fructosamine testing and its possible use to diabetes treatment in the future.

WHAT IS FRUCTOSAMINE?

A class of glycated proteins known as fructosamine is created when glucose non-enzymatically binds to serum proteins, mainly albumin. To reflect short-term glycemic management, it gives an estimate of the average blood glucose levels for the previous 2–3 weeks.[16] This is not the case for HbA1c, which is a longer-term indicator of glycemia that is created when hemoglobin in red blood cells glycated (2–3 months).

Biochemical Basis

The Maillard process, in which glucose binds to free amino groups on proteins, produces fructosamine. Throughout the course of these serum proteins' lifespan, the concentration of fructosamine is correlated with glucose levels.[17] Compared to HbA1c, which is impacted by the half-life of red blood cells (about 120 days), fructosamine offers a speedier reflection of glycemic alterations because albumin has a half-life of roughly 14–21 days.[18]

When a patient has hemoglobinopathies, is pregnant, or has a disease that affects red blood cell

turnover, for example, HbA1c may not accurately reflect glycemic control.[19] In these situations, fructosamine is especially helpful. Research findings indicate that fructosamine may serve as a valuable marker in groups where HbA1c is less accurate due to conditions such as anemia, chronic renal illness, and abrupt fluctuations in glucose levels.[20]

Fructosamine Versus HbA1c in Diabetes Diagnosis

Comparison of biomarkers

Glycated hemoglobin percentage in the blood is measured by HbA1c, an established biomarker for DM diagnosis and monitoring that represents long-term glycemic management.[21] HbA1c, however, has limitations in particular groups. Contrarily, fructosamine offers a quicker timescale for glycemic control assessment, which may be useful in some clinical contexts.

Advantages of fructosamine

1. Short-term glycemic control: Fructosamine can be used to track the success of short-term interventions such as dietary modifications, medication adjustments, or insulin therapy because it represents glucose management over the previous 2–3 weeks.[22]
2. Unaffected by red blood cell disorders: Patients suffering from hemoglobinopathies (such as sickle cell anemia or thalassemia), anemia, or recent blood transfusions may have erroneous HbA1c results. Because fructosamine is unaffected by the life span of red blood cells, it provides a dependable substitute in these situations.[23]
3. Cost-effectiveness: Because fructosamine testing is typically less expensive than HbA1c testing, it may be a good choice in environments with limited resources.[24]

Disadvantages of fructosamine

1. Lack of standardization: A major problem with fructosamine testing is that different facilities do not have the same standardized assays, which causes findings to vary.[25] It is challenging to develop global reference ranges as a result.
2. Influence of serum protein levels: Given that fructosamine is generated on blood proteins, diseases such as nephrotic syndrome or liver illness that impact protein concentrations might also change fructosamine levels, thereby causing misinterpretations.[26]

CLINICAL UTILITY OF FRUCTOSAMINE

In Specific Patient Populations

In patient populations where HbA1c may not offer an appropriate assessment of glycemic management, fructosamine is very helpful.

1. Pregnancy: HbA1c values may be impacted by elevated red blood cell turnover during pregnancy, which reduces its accuracy when used for glycemic monitoring in cases of gestational DM (GDM). It has been suggested that fructosamine be used to monitor glucose management in pregnant diabetic women, as it offers a more accurate representation of short-term glucose fluctuations.[27] Fructosamine is a more responsive biomarker that can be utilized by doctors to evaluate the efficacy of glycemic management in GDM, according to a study by Harper and Durnwald.[24]
2. Hemoglobinopathies: The decreased red blood cell survival in patients with hemoglobinopathies, such as sickle cell disease or thalassemia, can lead to erroneous findings on the HbA1c test. As a hemoglobin-independent measure of glycemic control in these populations, fructosamine is more precise.[28] Fructosamine, a useful substitute for HbA1c in sickle cell disease patients, has been demonstrated in a study by Collins and Evans to be a trustworthy marker.[19]
3. Renal disease: Red blood cell turnover is frequently affected in patients with chronic kidney disease (CKD), which can have an impact on HbA1c levels. As a more accurate measure of glycemic management in individuals with CKD, fructosamine – which represents the glycation of serum proteins – is unaffected by red blood cell turnover.[11]

PRACTICAL APPLICATION IN CLINICAL SETTINGS

To track brief variations in blood glucose levels, fructosamine testing can be included into clinical practice. When quick feedback is required, it can also be used to assess glucose control and track the effectiveness of treatment strategies such as adjustments to insulin therapy.[12] In patients with varying glucose levels as a result of hospitalization or serious illness, it has also been proposed as a tool for assessing glycemic control.[29]

RECENT ADVANCES AND LIMITATIONS

Technological Advances

The goal of recent fructosamine test advancements has been to increase the tests' accessibility and accuracy. There are now automated fructosamine assays that provide accurate and timely results. Clinicians now find it simpler to include fructosamine testing in their regular diabetic management.[17]

Limitations and Considerations

Clinicians should take into account the limits of fructosamine testing notwithstanding its benefits. Interpreting data can be complicated by the influence of serum protein levels, possible assay method variability, and disagreements over reference ranges.[13] Fructosamine testing should therefore be used in conjunction with HbA1c testing rather than as a substitute for it in the diagnosis and treatment of diabetes.

CONCLUSION

In DM, fructosamine is a useful biomarker for evaluating short-term glycemic control. It is a valuable tool in some clinical circumstances due to its advantages over HbA1c, especially in populations with diseases influencing red blood cell turnover. Even though fructosamine testing still has to be further standardized and validated, including it into routine diabetes treatment can improve the way people with diabetes are managed, especially in areas with limited resources or where quick glycemic evaluation is necessary.

CONFLICTS OF INTEREST

There was no conflicts of interest among the authors.

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