



# Ask An Endo

You asked how the results of fructosamine testing compares to that of HbA1c. Our Endos answered:

## Fructosamine as an Alternative Measure of Chronic Glycemia

*By: Sana Ghaznavi, Julie McKeen*

Measurement of glycemic control is a fundamental component of diabetes mellitus management. Several landmark studies have proven the importance of glycemic control in preventing the development of microvascular complications associated with chronic hyperglycemia.

Several methods of measurement of chronic glycemic control exist. These methods take advantage of the fact that glucose attaches itself to various proteins circulating in blood (a process known as “glycation”), thus altering these proteins in ways that can be measured. Hence, the greater the amount of glucose in the blood, the greater the amount of glycation that is measured.

The most widely used glycosylated protein is glycosylated haemoglobin, also known as HbA1c. HbA1c most accurately reflects the average glycemia over the last 3 to 4 months. While HbA1c is a commonly used and robust measure of glycemic control, it has certain limitations. The HbA1c is dependent on red blood cell turnover and is therefore vulnerable to conditions that increase or decrease red blood cell (RBC) turnover rate.

Common conditions leading to increased RBC turnover, and hence, falsely decreased HbA1c are recent blood loss or hemolysis, treatment of anemia with vitamin B12 or iron, chronic liver disease, chronic kidney disease, and hemoglobinopathies. Conditions leading to decreased RBC turnover, and therefore falsely increased HbA1c include anemia secondary to iron or B12 deficiency, alcoholism, or asplenic patients.

In situations where the HbA1c is less reliable, clinicians may prefer to use other measures of glycemic control, such as glycated albumin or fructosamine. Fructosamine is predominantly a measure of glycated albumin, along with several other glycated proteins. It reflects the average glycemia over 2 to 3 weeks.

Fructosamine levels must be interpreted in the context of a local reference range at each institution. As a general guideline, every 75  $\mu\text{mol}$  of fructosamine equates to roughly 3.3  $\text{mmol/L}$  of blood glucose, or 2% HbA1c. Fructosamine measurements are less reliable in conditions that alter protein metabolism (and therefore, albumin levels), such as nephrotic syndrome, liver cirrhosis, pregnancy, or malnutrition. Fructosamine also shows more within subject variation than HbA1c. Moreover, as most major studies of diabetes mellitus have used HbA1c as a marker of chronic glycemia, the linkage between fructosamine levels and average glucose or development of diabetes complications is less clear than for HbA1c.

#### Bottom line:

- HbA1c reflects the average glycemia over the last 2 to 3 months, whereas fructosamine reflects the average glycemia over the last 2-3 weeks
- Fructosamine can be used in situations of altered RBC turnover, when HbA1c is less reliable
- Fructosamine can also be used in situations where rapid evaluation of changes to glycemia are desired, such as when titrating diabetes medications
- Fructosamine measurements are less reliable in states of hypoalbuminemia
- The linkage between fructosamine and diabetes complications is less clear than for HbA1c, and HbA1c remains the preferred measurement of chronic glycemia in patients with a normal RBC turnover rate

#### References:

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Danese E, Montagnana M, Nouvenne A, and Lippi G. Advantages and Pitfalls of Fructosamine and Glycated Albumin in the Diagnosis and Treatment of Diabetes. *Journal of Diabetes Science and Technology*. 2015. 9(2):169-176.

