



FACULTAD DE QUIMICA
CENTRO NACIONAL DE INFORMACION QUIMICA

TEMA : FRUCTOSAMINE Y DIABETES

V.S

Fructosamine and glycated haemoglobin in the assessment of long term glycaemic control in diabetes.

Shield JP, Poyser K, Hunt L, Pennock CA

Fructosamine and glycated haemoglobin were measured simultaneously in 147 children with diabetes. If glycated haemoglobin is considered as the 'gold standard' for long term glycaemic control, then fructosamine is a poor indicator of actual glycated haemoglobin values, with wide 95% confidence (fiducial) limits. This shows that it is impossible to accurately predict glycated haemoglobin concentrations and therefore, by implication, longer term glycaemic control, from measurements of fructosamine. As the major studies on the prevention of microvascular complications in diabetes have used glycated haemoglobin levels to assess glycaemic control, it is suggested that this measurement should be used in all children with diabetes in preference to the measurement of fructosamine.

Pol Arch Med Wewn 1993 Sep;90(3):180-183

[Value of fructosamine test in monitoring of diabetes complicated by proteinuria].

[Article in Polish]

Ciechanowski K, Ciechanowicz A, Czekalski S

The aim of study was evaluation of fructosamine test in monitoring of diabetes mellitus complicated by proteinuria. Twenty patients with type 1 diabetes mellitus without proteinuria and 20 diabetic (type 1) patients with proteinuria were examined. Absent-present proteinuria was alone differential parameter between these groups. Correlations between past-glycaemia and other indices of diabetes balance as fructosamine, glycated haemoglobin and fructosamine: albumin molal ratio were examined. Results of study suggest that fructosamine test is useless in monitoring diabetes with proteinuria, but fructosamine: albumin molal ratio is a good parameter in monitoring of either: diabetes mellitus without proteinuria and with proteinuria.

Ginekol Pol 1995 Nov;66(11):605-608

[Use of fructosamine serum level measurements for diagnosis of insulin-dependent diabetic in pregnancy].

[Article in Polish]

Strojek K, Pietraszek F, Grzeszczak W, Wojcieszek K

In this study it has been tested the usefulness of serum glycosyl protein (fructosamine) to diagnose diabetic pregnant women requiring insulin therapy. The analysis was performed on the base of obtained results of glucose tolerance test, glycemia level in diurnal profile, fructosamine level and its relationship to albumin level and total protein amount in serum pregnant women with carbohydrates intolerance. Calculated specificity and sensitivity of above mentioned measurements was too low. We can not concluded that it is necessary to include insulin-therapy in diabetic pregnancy on the base of fructosamine serum level even corrected by protein or albumin serum level.

[Respective value of glycated hemoglobin and fructosamine assays in the care of diabetes mellitus].

[Article in French]

Bernard M, Bordas-Fonfrede M, Grimaldi A, Guillemin C, Stahl A, Leutenegger M, Gillery P

The monitoring of metabolic balance in diabetes mellitus involves the assay of cumulative markers of protein glycation. Glycated hemoglobin, particularly the major component HbA1c, and fructosamine, which reflects glycated plasma protein levels, are the most commonly used parameters. Nevertheless, their utilization is still under discussion with respect to methodologies used, as well as to their respective interest in clinical diabetology. This review shows current opinion concerning the analytical and physiopathological use of these biological indicators.

Publication Types:

- Review
- Review, tutorial

Nippon Koshu Eisei Zasshi 1994 Jan;41(1):67-73

[A method of estimation for prevalence of diabetes mellitus from fructosamine levels].

[Article in Japanese]

Hashimoto S, Nagai M, Sakata K, Yanagawa H, Sueta H, Tanaka T, Shirahama S

A method for estimating the prevalence interval of diabetes mellitus from fructosamine data is presented, which is based on the previously reported method for estimating prevalence from results of screening tests and on the results of 75 gram glucose tolerance test and fructosamine test in 1,359 examinees. Where true prevalences are 1-20% and population size is 100-10,000, the estimates for prevalence of diabetes mellitus are generally minimum when a screening level of 310 $\mu\text{mol/l}$ of fructosamine is utilized. In our method, a screening level for fructosamine of 310 $\mu\text{mol/l}$ was specified. Standard error ratios of estimated prevalence of diabetes mellitus to true prevalence in a population with an actual prevalence of 10% were about 40% for a population of 200 persons, and about 20% for 2,000 persons or more.

Clin Invest Med 1997 Apr;20(2):103-109

Variable glycation of serum proteins in patients with diabetes mellitus.

Couturier M, Amman H, Des Rosiers C, Comtois R

OBJECTIVE: To determine whether there were variations *in vivo* and *in vitro* in the glycation process among patients with diabetes mellitus and to assess the characteristics of patients with high and low glycation, if this was observed. **PATIENTS:** Patients ($n = 185$) attending a Diabetes Day Care Centre or Notre-Dame Hospital in Montreal participated in the *in vivo* study. Patients found to have high and low glycation were asked to allow the use of their serum for the *in vitro* part of the study.

INTERVENTION: Capillary blood glucose levels were determined by nursing staff 4 times a day over 7.3 (standard deviation [SD] 5.3) consecutive days with commercially available glucose oxidase reagent strips and meters. The ratio of the fructosamine concentration to the protein concentration (the F/P ratio) and the glycated hemoglobin were also determined at the same time as the capillary blood glucose level. Glycation was defined as the mean capillary blood glucose/F/P ratio. Patients with high and low glycation (higher or lower than [SD], of the mean) were compared. For the *in vitro* study, incorporation of carbon-14 glucose in serum proteins incubated with a 30-mmol/L glucose concentration was studied in some of the patients with low and high glycation. **RESULTS:** The mean capillary blood glucose/F/P ratio was a mean of 2.30 (SD 0.29) g/mL. Of the 185 subjects 31 had high glycation (1.46 [SD 0.19] g/mL) and 27 had low glycation (2.97 [SD 0.035] g/mL, $p < 0.001$). There was no significant difference in age, sex, diabetic treatment and glycated hemoglobin levels between the 2 groups. However, patients with low glycation had a greater body mass index (29.4 [SD 5.7] kg/m^2 v. 26.4 [SD 4.3] kg/m^2 , $p < 0.05$). *In vitro*, incorporation of ^{14}C glucose in serum proteins incubated with a 30mmol/L glucose concentration was higher in the 9 patients with high glycation than in that of the 7 with low glycation (0.031% [SD 0.03%] per gram of proteins v. 0.028% [SD 0.03%] per gram of proteins, $p < 0.02$).

CONCLUSIONS: Glycation may vary among patients with diabetes mellitus who have similar capillary blood glucose concentrations. Glycation appears to be lower in patients with a greater body mass index. Furthermore, alternation in the glycation process itself may explain, in addition to the mean blood glucose level, the difference in fructosamine levels.

Glycosylated hemoglobin and fructosamines: does their determination really reflect the glycemic control in diabetic patients?

Testa R, Testa I, Manfrini S, Bonfigli AR, Piantanelli L, Marra M, Pieri C

The present experiment was designed to determine whether scavenging capacity of serum, in addition to glucose level, influences hemoglobin and serum protein glycosylation in non-insulin dependent diabetic patients. For this purpose forty-seven patients homogeneous for age, disease duration, therapy and glyco-metabolic control were selected. Fasting and post-prandial glycemia and insulinemia as well as glycosuria were weekly analysed during the sixty days preceding glycosylated hemoglobin (HbA1c), fructosamines and serum scavenging capacity determination. This last parameter has been evaluated by a method based on the property of beta-phycoerythrin (beta-PE) to lose its fluorescence when damaged by oxygen radicals, that were produced by Cu⁺⁺ and H₂O₂. The oxygen radical absorbance capacity (ORACOH) of serum was assayed as the ability of serum to delay the loss of beta-PE fluorescence. As expected, a statistically significant positive correlation was found comparing both fructosamines and HbA1c levels with mean fasting glycemia measured over twenty and sixty days, respectively. The key result of this study is represented by the finding that both HbA1c and fructosamines levels show a statistically significant negative correlation with ORACOH values. This correlation can explain a large percent of the data dispersion occurring when ORACOH is not taken into account. In order to better describe the role of ORACOH, patients were separated into two sub-groups with an ORACOH lower (L-ORACOH) and greater (H-ORACOH) than 100 U/ml. Examining the correlation between mean fasting glycemia and the two glycosylated proteins considered in these two sub-groups, curves with different slopes were obtained, supporting that the rate of glycosylation of both proteins was higher in L-ORACOH patients as compared to those with H-ORACOH. Present data suggest that for a proper interpretation of the HbA1c and fructosamines data in diabetic patients, the scavenging capacity level of serum should be taken into account.

Methods Inf Med 1993 Apr;32(3):237-240

Criteria for screening diabetes mellitus using serum fructosamine level and fasting plasma glucose level. The Japanese Society of Multiphasic Health Testing and Services (JMHT), Fructosamine Working Committee.

Kasezawa N, Kiyose H, Ito K, Iwatsuka T, Kawai H, Goto Y, Kondo K, Sasamori N, Suzuki K, Suzuki T, et al

A screening method using serum fructosamine level and the fasting plasma glucose level was used for screening patients with diabetes mellitus. The criteria for positive tests recommended by the Japanese Society of Multiphasic Health Testing and Services were evaluated. It was found that levels for the serum fructosamine of 290 $\mu\text{mol/l}$ or higher (or, for the fasting plasma glucose of 110 mg/dl or higher) agreed with the standard oral glucose tolerance test in identifying patients with diabetes mellitus in 96.7% of cases, and the serum fructosamine test was simpler and less expensive.

Diabet Med 1994 Jan;11(1):50-56

Fructosamine in obese normal subjects and type 2 diabetes.

Ardawi MS, Nasrat HA, Bahnassy AA

The effect of various grades of obesity on serum fructosamine concentrations was studied in Type 2 diabetic (n = 105) and non-diabetic (n = 128) subjects. In obese diabetic and non-diabetic subjects (body mass index $\geq 30 \text{ kg m}^{-2}$), the concentration of fructosamine was markedly lower than that obtained for lean diabetic and non-diabetic subjects with similar glycaemic control. Stepwise multiple-regression analysis showed that fructosamine was associated with glycaemic control (as indicated by fasting plasma glucose and glycated haemoglobin), fasting triglycerides, and body mass index in both diabetic and non-diabetic subjects. In vitro studies showed marked decreases in both the extent of [¹⁴C]-glucose incorporation into plasma proteins and fructosamine production by incubated sera of obese patients whether diabetic or non-diabetic, with obese subjects with body mass index $> 40 \text{ kg m}^{-2}$ exhibiting the greatest decrease. In conclusion, serum fructosamine concentrations are shown to decrease in obese diabetic and non-diabetic subjects with body mass index $\geq 30 \text{ kg m}^{-2}$ giving rise to the underestimation of glycaemic control as indicated by fructosamine measurement. A change in the glycation reaction itself may be partly responsible for such decrease.

Kinetics of HbA1c, glycated albumin, and fructosamine and analysis of their weight functions against preceding plasma glucose level.

Tahara Y, Shima K

OBJECTIVE--To examine the kinetics of HbA1c, glycated albumin (GA), and fructosamine (FA) levels in response to plasma glucose change and their relationship with the preceding plasma glucose level.

RESEARCH DESIGN AND METHODS--The time courses of HbA1c, GA, and FA after acute glycemic normalization were observed in nine patients with newly diagnosed non-insulin-dependent diabetes mellitus and compared with theoretical ones. Their weight functions against preceding plasma glucose level were analyzed assuming a stepwise plasma glucose change and compared with the theoretical prediction. **RESULTS**--The fasting plasma glucose level was acutely normalized after admission with a half-time of 6.3 +/- 2.4 days (mean +/- SD). The HbA1c level decreased linearly during the initial 2 months with a half-time of 34.6 +/- 10.1 days, followed by a gradual decrease thereafter. GA and FA levels decreased very rapidly during the initial 2-3 weeks with half-times of 17.1 +/- 2.8 and 12.2 +/- 4.8 days, respectively, followed by a gradual decrease thereafter. The time courses of HbA1c, GA, and FA agreed well with theoretically estimated decay curves. Experimental values of weight functions against the preceding plasma glucose level agreed well with the theoretical prediction. The weight functions for glycated proteins had maximum values on the days just before the measurement of glycated proteins and gradually decreased with an increasing time interval. The lengths of the periods over which the weight functions for HbA1c, GA, and FA extend back were estimated to be roughly 100, 40, and 30 days, respectively. **CONCLUSIONS**--The levels of HbA1c, GA, and FA do not reflect the simple mean but reflect the weighted mean of the preceding plasma glucose level over a considerably longer period than was previously speculated.

Ann Clin Biochem 1993 May;30(Pt 3):260-264

Biological variation in glycated proteins.

Davie SJ, Whiting KL, Gould BJ

The high degree of individuality in the fructosamine assay has been ascribed to non-specific interferences in the assay. To investigate this, we measured the biological variability of 10 non-diabetic subjects using the fructosamine assay, the new fructosamine plus assay, glycated albumin and glycated total plasma proteins by affinity chromatography. The total variation of the two fructosamine assays was half that of the affinity chromatography assays. This was mainly due to the greater analytical imprecision of the affinity chromatography assays. The resulting high index of heterogeneity for both affinity methods makes it difficult to assess the significance of changes in serial results. The within-subject variation made a small contribution to the total variation for all the assays, and was particularly low for the fructosamine assays. This suggests that any non-specific component makes a constant contribution to the measured fructosamine activity in non-diabetic subjects. The fructosamine assays therefore have significant advantages over the affinity chromatography methods as indices of medium-term glycaemic control.

Pol Arch Med Wewn 1996 Mar;95(3):212-217

[Fructosamine in blood serum, binding and degradation of 125J-insulin by erythrocyte receptors in young persons with type I diabetes--effect of physical exercise].

[Article in Polish]

Rychlewski T, Szczesniak L

The aim of investigation was the determination of the effect of regular physical exercise of intensity 35% VO₂max on glycolysation of proteins, expressed by fructosamine concentration in blood serum and on insulin sensitivity of erythrocyte receptors in children with diabetes mellitus type I. The investigations were performed with 10 young persons with diabetes mellitus type I, during their sanatorium treatment. During 21 days the children effected every day a 20-minutes ergometric exercise of intensity equivalent approximately to 35% VO₂max. Before the 3-weeks therapy and after its termination the examined children have performed an ergometric test exercise, with collection of blood samples. Obtained results allow to ascertain, that regular aerobic exercise contributed to the growth of physical efficiency expressed by the VO₂max value, reduction in fructosamine level in blood serum, increase in insulin sensitivity of erythrocyte receptor and improved effort tolerance related to glycemia.

Glycated proteins as indices of glycaemic control in diabetic patients with chronic renal failure.

Morgan L, Marenah CB, Jeffcoate WJ, Morgan AG

This study investigates the reliability of glycated haemoglobin, measured by electroendosmosis or by affinity chromatography, fructosamine, and albumin adjusted fructosamine, as indices of glycaemic control in Type 1 diabetes complicated by chronic renal failure. Twenty uraemic diabetic patients took part in the study, including 5 patients managed conservatively, 6 on CAPD, 3 on haemodialysis, and 6 renal transplant recipients. Results were compared with those from 15 diabetic subjects with normal renal function. In renal patients, there was significant correlation between glycated haemoglobin measured by electroendosmosis ($r = 0.45$; $p = 0.04$) or by affinity chromatography ($r = 0.57$; $p = 0.01$) and mean capillary blood glucose concentrations over the previous 6 weeks. The regression equations did not differ significantly between subjects with renal failure and those with normal renal function, suggesting that similar ranges can be used in interpreting glycated haemoglobin results from each group of patients. Patients on haemodialysis may be an exception; there was evidence that glycated haemoglobin may be misleadingly low in such subjects. Fructosamine correlated significantly with mean blood glucose concentrations measured over the previous week in patients with normal renal function ($r = 0.75$; $p = 0.001$), but not in patients with chronic renal failure ($r = -0.1$; $p = 0.71$). Calculation of an albumin adjusted fructosamine result failed to improve the correlation with blood glucose concentrations. The use of fructosamine cannot be recommended as an index of glycaemic control in uraemic patients.

Publication Types:

- Clinical trial

Biol Pharm Bull 1993 Feb;16(2):195-198

A novel colorimetric method for determination of glycated protein based on 2-keto-glucose release with hydrazine.

Kobayashi K, Yoshimoto K, Hirauchi K, Uchida K

We tried to measure glycated proteins by a novel method based on colorimetry of 2-keto-glucose which is released from the glycated protein (ketoamine) on heating with hydrazine. Reaction conditions were optimized with glycated human serum albumin (glc HSA) as a model compound. Ketoamine reacted quantitatively with hydrazine on heating at 100 degrees C for 0.5 h, followed by heating with phenylhydrazine at 60 degrees C for 1 h. Glucose interference with the assay was eliminated by preincubation of the sample with glucose oxidase at 37 degrees C for 0.5 h. Time courses for the coloration of glc HSA and human serum showed a profile similar to that of N-p-tolyl-D-isoglucoamine under optimized reaction conditions. The lower limit for the assay of glc HSA was 0.7 microM. The serum level of glycated proteins measured by the present method correlated well with that (fructoamine value, microM) measured by the conventional method (nitroblue tetrazolium-reducing method) ($r = 0.92$, $n = 35$). In conclusion, the present method is a novel, highly sensitive and reliable one for measuring glycated proteins in biological samples.

Diabet Med 1997 Oct;14(10):819-831

Problems in the assessment of glycaemic control in diabetes mellitus.

Kilpatrick ES

The measurement of glycated haemoglobin and serum fructosamine to assess the recent glycaemic control of diabetic patients has become well established. Likewise, the monitoring of blood glucose using glucose test strips and meters has become popular in both the community and in the hospital inpatient environment. However, despite improvements in the methods of analysis, clinically inaccurate assessments of glycaemia can still occur. Specific problems such as the lack of standardization in assays are in the process of being resolved, but inherent difficulties associated with these measures remain. Clinicians should be aware that these tests still need to be interpreted in conjunction with clinical prudence.

Publication Types:

- Review
- Review, academic

Serum fructosamine as a screening test for diabetes in the elderly: a pilot study.

Cefalu WT, Ettinger WH, Bell-Farrow AD, Rushing JT

OBJECTIVE: To determine the value of serum glycated protein, measured as serum fructosamine, as a screening test for diabetes in the elderly. **DESIGN:** Cross-sectional pilot study. **SETTING:** Ambulatory research clinic in university setting. **PATIENTS:** One hundred fifty-seven consecutive community-dwelling participants in the Cardiovascular Health Study, average age 71.8 + 5 (mean +/- SD, range 65-88 years). **MEASUREMENTS:** Serum fructosamine levels (first and second generation assay) were obtained. All subjects who did not have a diagnosis of diabetes were given a 75-g glucose tolerance test (GTT). **RESULTS:** Twenty-six subjects (17%) (10 previously diagnosed, 16 undiagnosed and asymptomatic) had diabetes mellitus, and 38 subjects (24%) had impaired glucose tolerance by history or by the GTT (WHO criteria). Only the 16 asymptomatic diabetics were included in the analysis for the pilot study. There was a significant difference in the fasting fructosamine level between non-diabetics and asymptomatic diabetics for the first generation (2.06 +/- .21 vs 2.53 +/- .49 mMol/L, $P < 0.0015$) and second generation assay (221 +/- 27 vs 269 +/- 48 mMol/L, $P < 0.0012$). Receiver operator curves were constructed to evaluate the test characteristics of serum fructosamine. Using a point of $>$ or $= 2.3$ mMol/L for the first-generation assay, the sensitivity to detect asymptomatic diabetes was 75%, specificity 83%, and positive predictive value 35%. To detect both diabetes and impaired glucose tolerance using a cutpoint of $>$ or $= 2.3$ mMol/L, the sensitivity was 24%, specificity 95%, and positive predictive value 68%. Employing a cut point of 250 μ Mol/L for the second generation assay, the sensitivity to detect diabetes was 81%, specificity 87%, and positive predictive value 43%. However, to detect diabetes and glucose intolerance using the second generation assay, the sensitivity was 39% and specificity was 86%. **CONCLUSION:** This study demonstrated that a single measurement of either first or second generation fructosamine showed promise as a screening test for diabetes, but not impaired glucose tolerance, in older people.

Clin Biochem 1994 Oct;27(5):421-423

Influence of protein and albumin levels on serum fructosamine concentration in a diabetic patient with multiple myeloma.

Comtois R, Couturier M, Ammann H

Diabete Metab 1993 May;19(3):321-324

[Standardization of fructosamine assay].

[Article in French]

Gillery P, Delattre J, Plaquet R, Stahl A

Publication Types:

- Review
- Review, tutorial

PMID: 8405624, UI: 94009875

Ann Biol Clin (Paris) 1994;52(5):389-390

[Role of the determination of serum fructosamine in the screening of glucose intolerance].

[Article in French]

Ben Rayana MC, Aoun K, Achour A, Zouaghi H

Publication Types:

- Letter

PMID: 7856941, UI: 95160335