Effects of Albumin and Immunoglobulin A on Fructosamine Assay

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Serum fructosamine, albumin, and IgA were measured in three groups of human subjects: 54 nondiabetic normal individuals, 149 nondiabetic patients, and 149 diabetic patients. Normal subjects had significantly ($P < 0.05$) higher fructosamine (2.91, SD 0.33, mmol/L) than did nondiabetic patients (2.49, SD 0.46, mmol/L). Each of these groups had significantly ($P < 0.05$) lower fructosamine than did diabetic patients (3.76, SD 1.16, mmol/L). Increased fructosamine appeared to be associated with increases in both albumin and IgA. However, fructosamine was significantly ($P < 0.05$) correlated with neither albumin nor IgA in the normal group, with only albumin in the nondiabetic group, and with both albumin and IgA in the diabetic group. Selective combinations of these populations not only shifted these significances but also eliminated some of the correlations. Our results suggest caution regarding the diagnostic role and universality of fructosamine and of its correlation with IgA as indicated by others.

Additional Keyphrases: variation, source of diabetes

Measurement of glycated hemoglobin (Hb A1c) is a well-recognized method for determining long-term (six to eight weeks) average glycemia (1). However, total glycated protein measurement (the fructosamine assay) has been suggested as an indicator of short-term (one to three weeks) average glycemia (2–4). Because of the utility of the fructosamine assay for monitoring short-term glycemia, this assay has received wide acceptance for monitoring not only diabetes (2–4), but also gestational diabetes, because of the risk to the fetus of uncontrolled glycemia (3, 5, 6).

The method primarily used for fructosamine assay is that of Johnson et al. (7), who used nitroblue tetrazolium. The assay is simple and reliable, and because it is automated, can be done on an emergency basis (3, 4, 8). Although these features make the assay practical to perform, several reports indicate controversy regarding the effect of IgA on the assay: (a) Rodriguez-Segade et al. (8) suggested that because they found fructosamine to be affected by the IgA concentration, IgA should also be assayed if the fructosamine values are to be useful; (b) Lloyd and Marples (9) found no correlation between IgA and fructosamine in 51 nondiabetic patients; and (c) Rodriguez-Segade et al. (10) indicated that the absence of correlation in the study of Lloyd and Marples (9) reflected too small a sample size (38 instead of >50 if the 13 patients who had liver disease were excluded).

These studies included either only nondiabetic patients (9) or diabetic and nondiabetic patients combined (8). Given the differences in these two populations, we cannot rule out that the significance of correlation between IgA and fructosamine may depend on the population studied. Our first objective was to investigate this correlation individually in three separate populations—normal individuals with no evidence of diabetes, nondiabetic patients, and diabetic patients—and to determine the effect of various combinations of these populations on the statistical significance of this relationship.

A dependence of fructosamine measurements on albumin concentrations was also reported (11). According to some studies (11–13), a correlation between fructosamine and albumin exists. However, another study (14) reported the absence of this correlation, and still others (2, 15, 16) observed that although fructosamine values may not be valid in hypoaalbuminemia, in individuals with albumin >30 g/L (2) or >35 g/L (15), fructosamine values are independent of albumin concentrations. Because of these controversies and because hypoaalbuminemia is present in many of our diabetic patients (because they have renal and liver diseases), we required further investigation of the effect of albumin on the fructosamine assay before assay results could be released for clinical use. Our second objective was to determine the effect of albumin on the fructosamine assay in the three populations and in their various combinations as stated above.

Lloyd and Marples (9) suggested that the increase of fructosamine in liver disease occurs partly because of positive interference by bilirubin. However, in a previous study (15), they had concluded that serum from jaundiced subjects does not have significantly different fructosamine concentrations than serum from a reference group of normal subjects. Because of these conflicting observations, our third objective was to determine the effect of total bilirubin on the fructosamine assay.

Materials and Methods

Serum fructosamine was measured with an Abbott VP analyzer (Abbott Labs., N. Chicago, IL) by the nitroblue tetrazolium colorimetric procedure (17, 18) with use of the reagents, calibrator, and the protocol for the Abbott VP from Roche Diagnostics (Nutley, NJ). Glycohemoglobin in anticoagulated blood was assayed with the GlycoTek Affinity column method and reagents from Helena Labs (Beaumont, TX). Serum IgA was quantitated with the aca discrete analyzer, with

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1 The mention of a trade name does not imply endorsement: another suitable system may be equally effective for the assay.

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All analyses were done on the blood collected from fasting subjects. When not assayed on the day of collection, sera were stored at -20°C. All assays were completed within 1 week of collection. Three groups of subjects were included in the study. Group I (the normal subjects) included 54 healthy hospital staff members (47 men, 7 women; ages 22–69 years, mean 44, SD 12), medical students, and residents with no personal or family history of diabetes. Group II (the nondiabetic patients) included 149 ambulatory patients (145 men, 4 women; ages 21–98 years, mean 57, SD 15) with no history of diabetes and no renal or hepatic disease. Group III (the diabetic patients) included 149 ambulatory patients (146 men, 1 woman; ages 31–91 years, mean 62, SD 10) with clinically established (19) diabetes mellitus who had not been treated for diabetes before blood was collected for the tests here. In this group, 84 had no renal or liver disease, 50 had renal disease, and 15 had liver disease. Normal ranges for fasting blood glucose and glycohemoglobin in this laboratory were 3.6–6.0 mmol/L and 4–8%, respectively. All subjects in Groups I and II had normal values for fasting blood glucose and glycohemoglobin. All subjects in Group III had fasting glucose >11 mmol/L and glycohemoglobin >9.5%. The preponderance of men in the population studied reflects the patient population in VA hospitals.

We also compared the fructosamine concentrations measured in 18 diabetic patients, 9 of whom had above-normal total bilirubin (>17.1 μmol/L, range, 18.8–356.7) and 9 of whom had normal bilirubin concentrations (0–17.1 μmol/L).

All data from the three groups were used without exclusions for statistical analyses. The statistical significance of differences was determined at the 5% level by Student's t-test if distribution was Gaussian or by Wilcoxon test, which is resistant to outliers, if the population distribution was not Gaussian (20, 21). A reduction in the size of groups occurred once all diabetic patients were separated by presence of renal or liver disease. Our objective was to determine whether renal or liver disease in diabetic patients affected the fructosamine concentration in two respects: the effect of IgA on fructosamine and the effects of IgA and albumin on fructosamine. To accomplish this and to circumvent the loss of power of the Student's t-test associated with reduction of group size, we assessed the fructosamine results in groups with or without renal or liver disease by analysis of covariance according to diagnostic category, by using IgA as covariate in data set a and IgA and albumin as covariates in data set b (21). Correlation coefficients were tested for significance of difference at the 5% probability level (22, 22) and computed by Spearman's method (21, 23). Partial correlation and regression were computed as described (21, 23).

We used BMDP Statistical Software (BMDP Statistical Software, Inc., Los Angeles, CA) to perform stepwise discriminant analysis, which finds the combination of variables that best predicts the category or group to which a given case belongs. Here, the categories or groups were normal subjects, nondiabetic patients, and diabetic patients. The variables (also referred to as predictor variables) in our work were albumin, fructosamine, and IgA. The combination of predictor variables is called the classification (or discriminant) function. This analysis requires that the category of each case be identified. In stepwise discriminant analysis, the variable that adds the most to the separation of the groups is automatically entered into the discriminant function in a successive stepwise manner. The step before any variable enters the discriminant function is called step zero. At this step the analysis provides F-statistics on each variable, computed from one-way analysis of variance of a given variable for the groups used in the analysis. Stepwise discriminant analysis automatically evaluates the number of cases correctly classified into each group and performs "jackknife" validation to reduce bias in this evaluation. The analysis provides a summary of each step, including the F-value for the variable entered, the Wilks' Lambda or U-statistics, approximate F-statistics, and jackknifed classification. U-statistics are multivariate analysis of variance statistics that test the equality of group means for the variables in the discriminant function. Approximate F-statistics are transformed Wilks' Lambda statistics that can be compared with the F-value distribution; for example, at step 1 the F-statistic is the same as that in the one-way analysis of variance between the group means for the variable entered.

Results

The between-batch and within-batch precision values (CVs) for our fructosamine assay (n = 19; fructosamine = 2.4 mmol/L) were 5.7% and 1.3%, respectively. Table 1 lists the data on fructosamine in the various groups studied. Normal individuals had significantly (P < 0.05) higher fructosamine (2.91 mmol/L) than did the nondiabetic patients (2.49 mmol/L). Diabetic patients had significantly (P < 0.05) higher fructosamine concentrations than did either of these two groups. This was true not only for all diabetic patients (3.76 mmol/L), but also for diabetic patients without renal or liver disease (3.82 mmol/L), with only renal disease (3.72 mmol/L), with only liver disease (3.58 mmol/L), and with renal or liver disease (3.69 mmol/L). However, none of these five values differed significantly (P < 0.05) from each other. Although fructosamine increased with increases in albumin and IgA, groups differed in the significance of the correlation between fructosamine and each analyte. Thus, whereas fructosamine in all diabetic patients and in the diabetic patients without renal or liver disease was significantly correlated with both albumin and IgA (P < 0.05), it was significantly correlated (P < 0.05) with only albumin in the nondiabetic patients. Fructosamine was not significantly (P < 0.05) correlated with either
Table 1. Relationships of Fructosamine with Albumin and IgA in Serum of Normal Individuals and Nondiabetic and Diabetic Patients

<table>
<thead>
<tr>
<th>Subjects</th>
<th>n</th>
<th>Albumin, g/L</th>
<th>IgA, g/L</th>
<th>Fructosamine, mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal subjects</td>
<td>54</td>
<td>43 (3)</td>
<td>0.121</td>
<td>2.1 (0.8)</td>
</tr>
<tr>
<td>Nondiabetic patients</td>
<td>149</td>
<td>33 (8)</td>
<td>0.625*</td>
<td>3.5 (1.6)</td>
</tr>
<tr>
<td>Diabetic patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>149</td>
<td>35 (7)</td>
<td>0.320*</td>
<td>3.5 (1.6)</td>
</tr>
<tr>
<td>Without renal (R) or liver (L) disease</td>
<td>84</td>
<td>37 (6)</td>
<td>0.404*</td>
<td>3.4 (1.6)</td>
</tr>
<tr>
<td>With R disease only</td>
<td>50</td>
<td>34 (7)</td>
<td>0.195</td>
<td>3.5 (1.6)</td>
</tr>
<tr>
<td>With L disease only</td>
<td>15</td>
<td>30 (6)</td>
<td>0.422</td>
<td>3.7 (2.1)</td>
</tr>
<tr>
<td>With R or L disease</td>
<td>65</td>
<td>33 (7)</td>
<td>0.239</td>
<td>3.6 (1.7)</td>
</tr>
<tr>
<td>All normal subjects + nondiabetic patients</td>
<td>203</td>
<td>36 (8)</td>
<td>0.852*</td>
<td>2.3 (0.9)</td>
</tr>
<tr>
<td>All patients (diabetic + nondiabetic)</td>
<td>298</td>
<td>34 (7)</td>
<td>0.370*</td>
<td>2.9 (1.5)</td>
</tr>
<tr>
<td>All normal subjects + diabetic patients</td>
<td>203</td>
<td>37 (7)</td>
<td>0.086</td>
<td>3.1 (1.6)</td>
</tr>
<tr>
<td>All normal subjects and patients</td>
<td>352</td>
<td>36 (7)</td>
<td>0.299*</td>
<td>2.8 (1.4)</td>
</tr>
</tbody>
</table>

Mean (SD).

*Significantly (P < 0.05) correlated with fructosamine.

albumin or IgA in normal individuals or in diabetic patients if they had renal or liver disease.

The significance of these correlations in the various combinations is apparent in the correlation of fructosamine with IgA and albumin (Table 1). All pairs of variables that exhibited significant correlations in Table 1 retained this feature even in partial correlations. Conversely, no pair of variables that lacked significant correlation in Table 1 emerged with significant partial correlations.

Linear-regression analyses between fructosamine and albumin in the normal group, the nondiabetic group, and the diabetic patients group data shown in Table 1 gave the following results (±SE) for each group: y-intercepts of 2.35 (1.53), 1.22 (1.10), and 1.88 (1.37); slopes of 0.130 (0.149), 0.382 (0.099), and 0.537 (0.131); and standard errors of the estimate of each regression line of 0.330, 0.362, and 1.099, respectively. This statistical analysis between fructosamine and IgA for the corresponding groups produced y-intercepts of 2.93 (1.71), 2.51 (1.58), and 3.31 (1.82); slopes of 0.0001 (0.0006), 0.0001 (0.0004), and 0.0013 (0.001); and standard errors of the estimate of each regression line of 0.332, 0.464, and 1.14, respectively. Tests of statistical significance (at 5% level) of the difference of the slope from zero for each of the above regression lines gave the following results: between fructosamine and albumin the difference was significant only in nondiabetic and diabetic patients, and between fructosamine and IgA this difference was significant only in the diabetic patients. Hence, significant direct relationships existed between fructosamine and albumin only in the patients (nondiabetic and diabetic) and between fructosamine and IgA only in the diabetic patients. A scatter plot of fructosamine vs albumin (Figure 1) further demonstrates the direct relationships between these two analytes in the nondiabetic and diabetic patients.

The normal range for albumin in our laboratory was 30–60 g/L. The lowest albumin concentration in the normal group was 37 g/L. Hence, to compare our values with those in literature, both groups of patients were divided into four groups by albumin concentration: (a) below the lower limit of the normal range (<30 g/L); (b) in the normal range (≥30 g/L); (c) between the lower limit of normal and the lowest concentration seen in the normal subjects group (≥30 to <37 g/L); and (d) ≥37 g/L. No individual in the study had albumin >50 g/L. The fructosamine concentration in each group is summarized in Table 2. A statistically significant (P < 0.05) correlation between albumin and fructosamine existed only in some of the albumin groups: in nondiabetic patients in groups a and b; in all diabetic patients in group b only; in no diabetic patients without renal or liver disease; and in diabetic patients with renal or liver disease.

Fig. 1. A scatterplot of fructosamine vs albumin in the three patient groups: △, normal; ○, nondiabetic, and ⋄, diabetic.
disease only in group b. Note that in this last case, the correlation between albumin and fructosamine was significant despite its lack of significance in the group of diabetic patients with renal or liver disease (Table 1). Conversely, although the entire group of diabetic patients without renal or liver disease showed a significant correlation between albumin and fructosamine (Table 1), when this group was divided into subgroups by albumin concentration, no significant correlation emerged. Furthermore, absence of a significant correlation here between albumin and fructosamine in nondiabetic and diabetic patients in group d suggested that with respect to this correlation, these two groups were similar to the group of normal individuals. Computation of even the partial correlations on the pairs of variables referred to here did not alter the above conclusions regarding significance of correlations.

The normal range of IgA in our laboratory was 0.57–4.1 g/L. For comparisons we grouped the diabetic patients into normal (a) and abnormal (b) categories based, respectively, on IgA concentrations ≤4.1 and >4.1 g/L. Normal subjects and nondiabetic patients had only normal concentrations of IgA.

To determine the effect of renal and liver diseases on this IgA-associated increase in fructosamine (shown also by regression analysis previously), the diabetic patients without renal or liver disease were separated (as shown in Table 3) from those with one of these diseases and further separated by IgA concentration. Then the differences in the resulting four fructosamine values were evaluated by analysis of covariance by diagnostic subcategory, with IgA as covariate. This analysis showed that the fructosamine concentration was not affected by renal or liver disease but was affected by the concentration of IgA. There was no significant correlation (or partial correlation) between IgA and fructosamine in any of the IgA-concentration-based groups in Table 3.

As already apparent from regression analysis, fructosamine increased with increases in albumin and IgA (Table 4). To assess the relative influences of albumin, IgA, and diagnostic subcategories (Groups II and III in
Table 4) on fructosamine, we evaluated eight fructosamine values in these two subgroups by analysis of covariance with albumin and IgA as covariates. This analysis demonstrated that renal or liver disease did not affect the fructosamine concentration; instead, fructosamine was affected by albumin and IgA concentrations.

For discriminating diabetic patients (D) from normal individuals (N), the three variables with respect to their prediction values (Table 5) were in the following order: albumin (Alb) > fructosamine (Fr) > IgA. This order was Fr > IgA > Alb in discriminating (Table 5) D from nondiabetic patients (ND). These sequences, respectively, were steps 1, 2, and 3 in the corresponding analyses (Table 5). In N vs D, although only 61.7% of the diabetic patients were correctly classified at step 1, this value increased to 79.2% and 79.9% in steps 2 and 3, respectively (Table 5). This suggested that in N vs D, although Alb was the best predictor of diabetes, Fr gave further enhanced prediction by 17%, with IgA improving it only by 0.7% (Table 5). In ND vs D, although Fr was the best (65.1%) predictor of diabetes, IgA increased it to 69.1% with no further increase due to Alb (Table 5). Thus, 20% and 31% of diabetic patients were, respectively, classified as normal individuals and nondiabetic patients even after all three variables had been entered into the discriminant analyses (Table 5). In contrast, 98.1% of normal individuals were classified as normal individuals and 95.3% of nondiabetic patients were classified as nondiabetic patients when all three variables were present in the analysis (Table 5). The above observation that in the fructosamine test up to 31% of diabetic patients appeared to be nondiabetic patients suggested the need for caution when using this assay for diagnostic purpose. Because fructosamine concentrations (Table 1) differed significantly between normal and nondiabetic groups, normal ranges (mean ± 2 SDs) were calculated separately for these two groups. For normal subjects the range was 2.3–3.6 mmol/L, whereas for nondiabetic patients it was 1.6–3.4 mmol/L.

Fructosamine (mmol/L), total bilirubin (µmol/L), albumin (g/L), and IgA (g/L) values, respectively, in diabetic patients with elevated total bilirubin concentrations were [mean (± SD): 3.9 (1.1), 64.0 (78.7), 30 (5), and 3.6 (2.2) and in diabetic patients with normal total bilirubin concentrations were 3.5 (1.0), 8.9 (3.8), 35 (8), and 3.5 (0.9). The diabetic subjects with elevated total bilirubin did not have significantly (P <0.05) different fructosamine concentrations than did the albumin- and IgA-matched diabetic patients with normal total bilirubin.

Discussion

The between-batch (5.7%) and within-batch (1.3%) CVs of our fructosamine assay are comparable with the values reported by others: 3% (24), 4.1% (18), 4.7–6.6% (12), 6.5% (7), and 7.4% (4) for between-batch CVs and 1% (24) and 2.1–3.3% (12) for within-batch CVs. Furthermore, our fructosamine values of 2.49 mmol/L for nondiabetic patients and 2.6 mmol/L for all normal subjects plus nondiabetic patients are comparable with the 2.4 mmol/L of Rodriguez-Segade et al. (8) and the values (2.2–2.5 mmol/L) from other authors, compiled previously (8).

Lloyd and Marples (9) noted an absence of correlation between fructosamine and IgA in nondiabetic patients. Our results agree with this finding, not only for nondiabetic patients but also for normal individuals. Lloyd and Marples (9) did not study diabetic subjects. In

Table 5. Summary of Stepwise Discriminant Analysis between Normal (N) and Diabetic (D) Groups and between Nondiabetic (ND) and D Groups

<table>
<thead>
<tr>
<th>Step no.</th>
<th>Variable entered</th>
<th>F* value to remove</th>
<th>U-statistic</th>
<th>Approx. F-statistic</th>
<th>df</th>
<th>Group</th>
<th>Percent correct</th>
<th>No. of cases classified into group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between N and D</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Alb</td>
<td>59.4</td>
<td>0.772</td>
<td>59.4</td>
<td>1 201</td>
<td>N</td>
<td>90.7</td>
<td>49</td>
</tr>
<tr>
<td>2</td>
<td>Fr</td>
<td>51.2</td>
<td>0.615</td>
<td>62.7</td>
<td>2 200</td>
<td>N</td>
<td>96.3</td>
<td>52</td>
</tr>
<tr>
<td>3</td>
<td>IgA</td>
<td>3.7</td>
<td>0.603</td>
<td>43.6</td>
<td>3 199</td>
<td>N</td>
<td>98.1</td>
<td>53</td>
</tr>
<tr>
<td>Between ND and D</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Fr</td>
<td>155.4</td>
<td>0.656</td>
<td>155.4</td>
<td>1 296</td>
<td>ND</td>
<td>90.6</td>
<td>135</td>
</tr>
<tr>
<td>2</td>
<td>IgA</td>
<td>20.9</td>
<td>0.612</td>
<td>93.4</td>
<td>2 295</td>
<td>ND</td>
<td>94.0</td>
<td>140</td>
</tr>
<tr>
<td>3</td>
<td>Alb</td>
<td>1.2</td>
<td>0.610</td>
<td>62.7</td>
<td>3 294</td>
<td>ND</td>
<td>95.3</td>
<td>142</td>
</tr>
</tbody>
</table>

*The order in which the given variable was entered into the discriminant function.

a Alb, albumin; Fr, fructosamine.

Values of F at Step 0 for N vs D analysis were 59.4 for Alb, 34.4 for IgA, and 28.9 for Fr; for ND vs D analysis, these values were 155.4 for Fr, 55.0 for IgA, and 4.4 for Alb.

* Done automatically by the computer.
normoglycemic subjects, Rodriguez-Segade et al. (10) found a significant correlation between IgA and fructosamine. Our results do not agree with this observation. These authors (8, 10) also observed a significant correlation between IgA and fructosamine in a population containing both nondiabetic and diabetic patients. Our results agree with this observation, not only in a population (nondiabetic and diabetic patients) comparable with theirs (8), but also when diabetic patients were considered alone (all or only those without renal or liver disease) or as a group made of all normal individuals plus nondiabetic patients plus diabetic patients.

Rodriguez-Segade et al. (8) postulated that a significant correlation between fructosamine and IgA occurs because of the greater reactivity of IgA toward nitroblue tetrazolium or a greater propensity of IgA to glycate. Their rationale of greater reactivity of IgA toward nitroblue tetrazolium was ruled out previously (9). Their second postulate also is not valid because Zoppi et al. (25) observed that of the two proteins, albumin and not IgA has a higher glycation rate, and in each of the seven populations that we studied (Table 1), our results support those of Zoppi et al. Our observations of no significant correlation between IgA and fructosamine in populations as large as 54 and 149 (Table 1) rules out their further contention (10) that population size of >51 is required for the correlation to be significant. Apparently resolving the differences between our findings on IgA and fructosamine correlation with those of Rodriguez-Segade et al. (8) may require consideration of our results regarding effect of case mix on this correlation. Because we observed that a significant correlation between these two variables can be changed simply by altering the case mix, there is no certainty that two separate laboratories will get identical results if their case compositions are not identical. Hence, the type of differences that exist between our results and those of others (8) regarding this correlation may persist. The fact that use of identical populations will resolve this controversy is apparent from similarity of our results with those of Rodriguez-Segade et al. (8) when similar populations (nondiabetic and diabetic patients) are compared.

We divided our population so that the albumin concentrations of our subgroups are comparable with published values. Doing so led to a decrease in group sizes, which in turn may have affected the statistical significance of correlations. Our results of significant correlation between albumin and fructosamine in nondiabetic patients with albumin <30 g/L (2, 11) and with albumin ≥30 g/L agree with those of others (2, 11). Our observation of no significant correlation between these two variables in nondiabetic patients with albumin ≥37 g/L is consistent with the results of others (15). The significant correlation between albumin and fructosamine appears to be specific for the normal concentration range of albumin (30–50 g/L). Thus, the significant correlation between albumin and fructosamine that we observed in all individuals with albumin ≥30 g/L appears to be eliminated by grouping subjects by albumin concentrations ≥30 to <37 g/L and ≥37 g/L. This may partly explain why in nondiabetic patients with normal albumin concentrations (≥30 g/L) this correlation is significant in our study but not in others (2, 11, 15) where the normoalbuminemic individuals may have had albumin concentrations in a range (≥30 to <37 g/L or ≥37 g/L) lacking this correlation.

In diabetic patients, we find a significant correlation between albumin and fructosamine only in the group with albumin ≥30 g/L, but not in those with albumin ≥30 to <37 g/L, ≥37 g/L, or <30 g/L. To our knowledge only one brief report (14) has appeared regarding correlation between these two variables in diabetic patients. In this group there was no significant correlation between these two variables whether the albumin concentration was >30 g/L or <30 g/L. However, the actual albumin concentration of the population with albumin >30 g/L was not reported. Consequently, the absence of this correlation may be because they only studied patients with selective (≥30 to <37 g/L or ≥37 g/L) albumin concentrations, which even in our study do not exhibit this correlation. Our normal range for albumin (30–60 g/L) seems surprisingly low. However, it is comparable with the prevailing albumin range of 32–55 g/L (26–28).

We observed that even a greater than sevenfold increase in total bilirubin does not cause significant increase in fructosamine when compared with a group with comparable albumin and IgA concentrations but normal total bilirubin. This agrees with the results of others (15) and rules out interference by bilirubin with the fructosamine assay. It was speculated that liver-disease patients have higher fructosamine concentrations, partly because of positive interference by bilirubin with fructosamine (9); because bilirubin and fructosamine data on individuals with comparable concentrations of IgA and albumin but normal bilirubin were not provided, this claim cannot be verified. Our results (Table 1) do not show that patients with liver disease have higher fructosamine concentrations than do those without liver disease.

Stepwise discriminant analysis revealed that on the basis of fructosamine concentration, in some population groups up to 31% of diabetic patients appear to be normoglycemic. Thus, to use fructosamine for diagnosing diabetes, caution is required, including establishing the normal concentration range for a population with serum albumin and IgA values comparable with those in the diabetic patients being diagnosed.

References
proteins

glycated

15.

serum

14.

13.

9.

Effects

diabetic

approach

11.

10.

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ayne

al.

5.


