COMPARISON OF SERUM FRUCTOSAMINE AND BLOOD GLUCOSE CONCENTRATIONS AS INDICES OF GLYCAEMIC CONTROL IN NON-INSULIN DEPENDENT DIABETIC OUT-PATIENTS

T O Lim, T Selvan, A Suppiah, N Khan, F Ismail

ABSTRACT

The usefulness and validity of blood glucose measurement as an index of diabetic control were assessed with reference to serum fructosamine. Two hundred and twenty-eight non-insulin dependent diabetic out-patients were studied in the usual clinical setting. Fasting blood glucose (FBG) concentration was positively correlated with serum fructosamine ($r=0.42$, $t=6.78$ $p<0.01$). On the basis of their serum fructosamine concentrations, patients were divided into 3 groups. They were good control (fructosamine ≤ 288 umol/l), acceptable control (fructosamine ≤ 320 umol/l) and poor control groups (fructosamine > 320 umol/l). The mean fasting blood glucose concentration was significantly higher in the latter than the former 2 groups. However, at each level of control, there was a wide range of FBG concentrations. Thus, the value of FBG in predicting glycaemic control is limited. Its positive predictive value was only 32%, and its overall accuracy as an index of diabetic control was only 58% though its negative predictive value was high (93%). In 162 patients with poor diabetic control as indicated by their serum fructosamine concentrations, 81 (50%) of them had FBG less than 10 mmol/l on their clinic visit day.

Fasting blood glucose is therefore not a reliable measure of good diabetic control, though it is useful in predicting poor control. FBG is simple to measure, cheap and rapidly available on clinic day, thus ensuring its continuing use. Doctors should be aware of its limitations and should not rely solely on FBG to assess diabetic control.

Keywords: Non-insulin dependent diabetes, control, serum fructosamine, fasting blood glucose

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INTRODUCTION

Current consensus view holds that diabetes specific complications can be prevented by attainment of normal or near normal metabolic control of the disorder[1]. In routine clinical practice it is therefore highly desirable to have a simple reliable test of metabolic control to permit frequent monitoring of patient's diabetes. The traditional test is blood glucose measurement. In our practice, we routinely measure the fasting and timed post-prandial blood glucose concentrations of diabetic out-patients. Blood glucose concentrations fluctuate throughout the day and a spot sample cannot be expected to characterise glycaemic state accurately, particularly in the insulin dependent diabetic with highly labile blood glucose levels. In non-insulin dependent diabetics, however, blood glucose levels, especially in the fasting state have been shown to be stable[2-4], presumably because of their greater residual endogenous insulin secretion. Fasting blood glucose concentration is therefore widely regarded as an accurate measure of glycaemic control in non-insulin dependent diabetic[5,6]. In the last 15 years, glycosylated protein measurement has become widely accepted as a useful alternative measure of diabetic control[7,8]. We recently acquired the ability to measure serum fructosamine. This offers us an opportunity to critically evaluate the validity of blood glucose measurement as an index of diabetic control.

METHODS

Diabetic patients were recruited for the study during their routine visit to the diabetic out-patient clinic of a hospital. All patients had previous venous whole blood glucose concentrations greater than 10 mmol/l on at least 2 occasions, in keeping with the WHO diagnostic criteria of diabetes[9]. All patients were treated by diet alone or by diet plus oral hypoglycaemic agents.

Patients were requested to fast overnight and to attend the diabetic clinic before breakfast. Blood specimens were obtained by venipuncture each for determination of fasting blood glucose (FBG) and serum fructosamine concentrations. A second specimen was taken approximately two hours after patients had taken their breakfast for determination of post-prandial blood glucose (PPBG) concentrations.

Forty-one healthy non-diabetic volunteers (age range 27 - 50 years, mean age 37 years; 22 men and 19 women) were recruited from hospital staff. Serum fructosamine concentrations were measured in these subjects to determine the normal reference range of serum fructosamine concentrations.

Medical Unit
Mentakab District Hospital
28400 Mentakab
Pahang
Malaysia

T O Lim, MBCHB(Glas), MRCP(UK)
Physician

T Selvan, MBBS
Medical Officer

A Suppiah, MBBS
Medical Officer

N Khan, MBBS
Medical Officer

F Ismail, MD(UKM)
Medical Officer

Correspondence to: Dr T O Lim
Clinical Specialist
Jabatan Nefrologi
Hospital Besar, Jalan Pahang
50586 Kuala Lumpur
Malaysia

Fig 1 - Correlation between Serum Fructosamine (FRUC) and Fasting Blood Glucose (FBG) concentrations

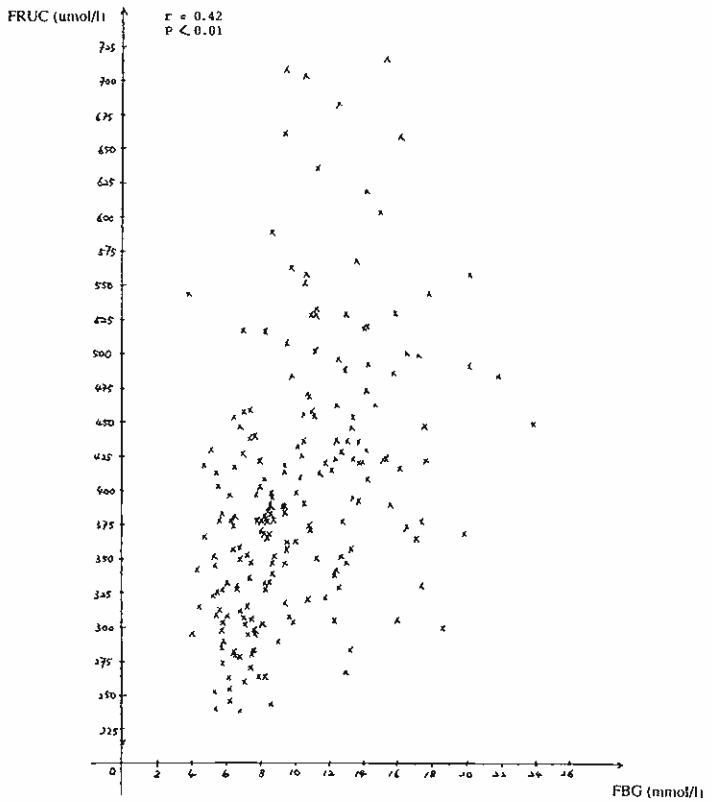

Fig 2- Correlation between Serum Fructosamine (FRUC) and two hour Post-prandial Blood Glucose (PPBG) concentrations.

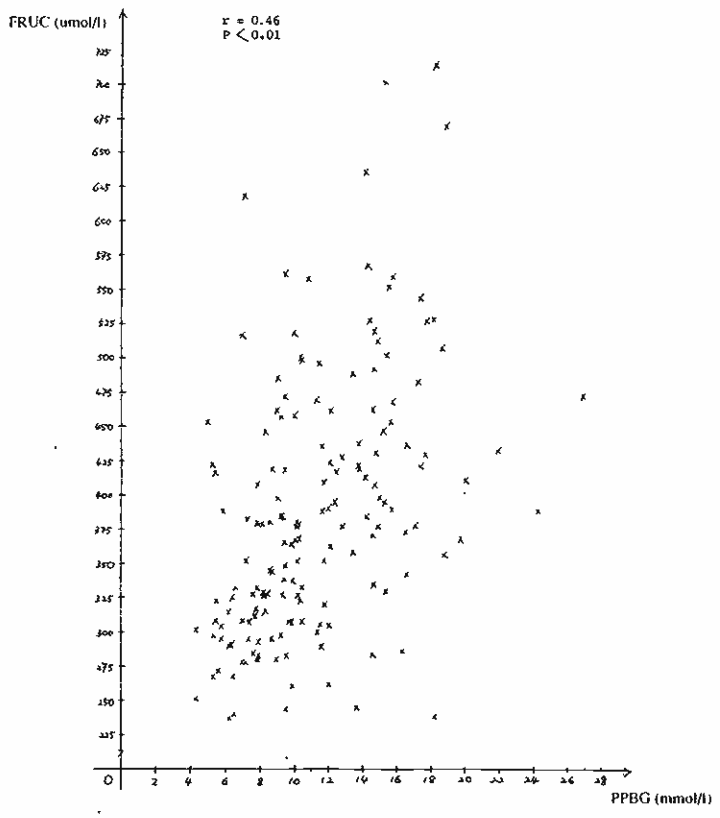

Table I - Relationship between status of metabolic control and mean Fasting Blood Glucose

Metabolic Control	No. of patients No (%)	Mean fasting BG mmol/l ± 1 SD	P
Good control Fructosamine ≤ 288 umol/l	20(10)	7.3 ± 2.2	t = 1.0512 P > 0.05
Acceptable control Fructosamine ≤ 320 umol/l	25(12)	8.2 ± 3.4	t = 3009 p < 0.01
Poor control Fructosamine > 320 umol/l	162(78)	10.1 ± 3.8	
Total	207(100)		

Table II - Validity of Blood Glucose Concentration as a measure of metabolic control, with reference to Serum Fructosamine

Metabolic Control	Good/Acceptable Fructosamine ≤320 umol/l	Poor Fructosamine >320 umol/l	
Good/Acceptable FBG ≤ 10 mmol/l	39	81	120
Poor FBG > 10 mmol/l	6	81	87
	45	162	207

Positive predictive value = proportion of those with FBG ≤ 10 mmol/l who had Good/Acceptable metabolic control as indicated by their serum fructosamine = 39/120 = 32%

Negative predictive value = proportion of those with FBG > 10mmol/l who had poor metabolic as indicated by their serum fructosamine = 81/87 = 93%

Accuracy = proportion of patients correctly identified as having Good/Acceptable or poor metabolic control = $\frac{39 + 81}{207}$ = 58%

Blood glucose concentrations were determined by a glucose oxidase method using Beckman Glucose analyser II. Serum fructosamine concentrations were determined by nitro-blue tetrazo-lium calorimetric assay[10,11] (Roche-Diagnostic) using Abbott VPSS autoanalyser.

Results were entered into a computer using D-Base III plus appplication programme for data collation and analysis. Statistical analysis was performed by linear regression analysis or student's t test where appropriate.

RESULTS

A total of 228 patients were studied. Their mean age was 53 years, range 24-81 years. There were 119 men and 109 women. Serum fructosamine results were available from all patients, while only 207 fasting blood glucose (FBG) and 162 post-prandial blood glucose (PPBG) results were available. Data analysis was done on those whose results were available.

Fig 1 and 2 show respectively the correlation between serum fructosamine and FBG, and between serum fructosamine and PPBG. The correlations were weak (fructosamine VS FBG, r=0.42, fructosamine VS PPBG, r=0.46) though they were statistically significant (t=6.78 and 6.48 respectively, P<0.01).

The range of serum fructosamine in 41 healthy volunteers was 217 to 283 umol/l (mean ± 1SD = 256 ± 16umol/l, coefficient of variation 6.2%). On the basis of a recent European Diabetes Study Group recommendation on targets for diabetic control[1], we defined good metabolic control as serum fructosamine less than or equal to 288 umol/l (mean + 2SD), and acceptable metabolic control as serum fructosamine less than or equal to 320 umol/l (mean + 4SD) and/or fasting blood glucose less than or equal to 10 mmol/l. On the basis of their metabolic control, patients can be divided into 3 categories. These are good control, acceptable control and poor control groups (serum fructosamine > 320 mmol/l). As shown in Table I, the mean fasting blood glucose concentration varies from 7.3 mmol/l for the good control group to 10.1 mmol/l for the poor control group. The difference in mean fasting blood glucose between good and acceptable control groups was not significant ($t = 1.051$, $P > 0.05$). That between acceptable and poor control groups was however highly significant ($t = 3.009$, $P<0.01$). Nevertheless, the standard deviations of fasting blood glucose concentrations were large indicating a wide range of blood glucose concentrations at each category of metabolic control.

The validity of blood glucose concentration as an index of diabetic control was assessed using serum fructosamine as the standard of reference. As shown in Table II, the positive predictive value of blood glucose measurement is only 32% and its overall accuracy only 58%. The table also shows that of 162 patients who had poor control as indicated by their serum fructosamine concentrations, only 81 of them (50%) had FBG less than 10 mmol/l on their clinic visit days.

DISCUSSION

In this country, the metabolic control of diabetic patients is currently assessed principally by blood glucose measurements at the out-patient clinic. An alternative test, the serum fructosamine assay is now commercially available. Blood glucose measurement is however likely to remain the routine test of diabetic control simply because it is much cheaper and technically simpler. Glycosylated protein measurement on the other hand is expensive and technically exacting. Its usefulness in insulin-dependent diabetics is proven[12,13]. Insulin dependent diabetes however is rare in Malaysia[14]. The vast majority of diabetics on follow-up at our clinic are non-insulin dependent. In these patients, the usefulness of routine testing of serum fructosamine remains uncertain[15], as fasting blood glucose is widely regarded as a valid and reliable measure of diabetic control [4-6, 15-17].

The results of this study show that blood glucose concentrations on clinic day were positively correlated with serum fructosamine. However, at each level of control as indicated by serum fructosamine, there was a wide range of FBG concentrations. Thus, any individual blood glucose measurement was of limited value in predicting glycaemic control. Indeed, its positive predictive value was only 32%, though its high negative predictive value (93%) was useful in identifying those with poor metabolic control.

Other studies[15,16] had however shown that FBG is a reliable and adequate measure of metabolic control. This is in contrast with our results. The discrepancy between our results and that of others is probably due to differences in patients' behaviour. It is well known that patients' behaviour preceding and on clinic visit days may differ from ordinary days. Patients may restrict food intake or may be more compliant with medication in the few days preceding clinic visit in order to lower their fasting blood glucose, thus giving spuriously good control. The extent of such attempted deception is uncertain and likely to vary widely among populations thus accounting for the discrepancy between our results and that of others. This is also the presumed explanation for the finding in this study of 162 patients with poor control as indicated by their serum fructosamine (which is a measure of average blood glucose concentration over the preceding 2-3 weeks), and yet 81 (50%) of them had FBG less than 10 mmol/l on their clinic visit days.

In conclusion, this study has shown that FBG is not an accurate measure of diabetic control. FBG may still be useful in predicting poor control. The technical simplicity of FBG measurement, its low cost and the rapid availability of FBG result on clinic day will probably ensure its continuing use. Doctors who care for diabetic patients should however be aware of the limitations of FBG and should not rely solely on FBG to assess diabetic control.

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REFERENCES

1. Alberti KGMM, Gries FA: Management of non-insulin dependent Diabetes mellitus in Europe: A consensus view. Diabetic Med 1988;5:275-81.
2. Turner RC, Holman RP: Insulin rather than glucose haemostasis in the pathophysiology of diabetes. Lancet 1976;i:1272-4.
3. Holman RK, Turner RC: Maintenance of basal plasma glucose and insulin concentrations in maturity onset diabetes. Diabetes 1979.28:227-30.
4. Holman RK, Turner RC: The basal plasma glucose: A simple relevant index of maturity onset diabetes. Clin Endocrinol 1980,14:279-86.
5. Alberti KGMM, Hockaday DR: Diabetes Mellitus. In: Weatherall DJ, Ledingham JGG, Warrell DA. eds. Oxford Textbook of Medicine. Oxford University Press 1986:51-101.
6. Howe Davies S, Simpson RW, Turner RC: Control of maturity onset diabetes by monitoring fasting blood glucose and body weight. Diabetes Care 1980;3:607-10.
7. Genen B, Rubenstein AH: Haemoglobin A_1: An indicator of the metabolic control of diabetic patients. Lancet 1977;ii:734-7.
8. Editorial. Haemoglobin A_1 and diabetes. Br Med J 1980,281:1304.
9. WHO Study Group. Diabetes Mellitus. WHO Technical Report Series 727;1985.
10. Johnson RN, Metcalf PA, Baker JR: Fructosamine: A new approach to the estimation of serum glycosylprotein: An index of diabetic control. Clin Chem 1982; 127: 87-95.
11. Kruse-Jarres JD, Jarauseh J, Lehmann P, Vogt BW: A new calorimetric method for the determination of fructosamine. Sonderdruck aus Lab Med 1989;13:145-53.
12. Northan DM, Singer DE, Hurxthal K: The clinical information of the glycosylated haemoglobin assay. N Engl J Med 1984;288:1484-6.
13. Baker JR, Metcalf PA, Holdaway IM, Johnson RN: Serum fructosamine concentration as measure of blood glucose control in Type I (Insulin dependent) diabetes mellitus. Br Med J 1985;290:352-5.
14. Lim TO: Prevalence, age at diagnosis, clinical characteristics and treatment of diabetes in the young in Pahang, Malaysia. Diabetes Res Clin Pract 1991. (In Press).
15. Mccance DR, Ritchie CM, Kennedy L: Is HBA_1 measurement superfluous in NIDDM? Diabetes Care 1988;11:512-4.
16. Pecoraro RE, Koepsell TD, Chen MS, Lipsky BA: Comparative clinical reliability of fasting plasma glucose and glycosylated haemoglobin in non-insulin dependent diabetes mellitus. Diabetes Care 1986;9:307-15.
17. Muii A, Howe Davies BA, Turner RC: General practice care of non-insulin dependent diabetes with fasting blood glucose measurement. Am J Med 1982;73:637-40.