



Glycosylated Haemoglobin (Hb A1) In Aeromedical Evaluation of Diabetes Mellitus and Impaired Glucose Tolerance

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Proper assessment of glycaemic control is essential in the management of diabetes mellitus. Estimation of GHb gives a better indication of the long term blood glucose levels rather than isolated blood glucose estimations. The study comprised of 48 male subjects reporting for medical boards and 17 healthy adults as controls. The GHb values correlated well with the post prandial blood sugar levels. The values of GHb noted in this study in healthy controls and diabetics are comparable to those reported in literature.

Introduction

The basic controversy, about basement membrane changes in vascular and neurological lesions of diabetes mellitus, whether they are true complication of diabetic state or due to separate defect, has attracted lot of attention. The difficulty in assessing the control of diabetes in an individual by estimation of blood glucose levels alone has led many workers to search for better methods of evaluation. Investigations of the structures and biosynthesis of glycosylated haemoglobin in the past decade, have provided a means to objectively assess the average level of glycaemia in diabetic patients.

Cation exchange chromatography of haemolysate of human erythrocyte, resolves into four negatively charged minor Hb, from main HbA. These components (HbA1a, HbA1a², HbA1b and HbA1c) are collectively referred to as HbA1 or glycosylated Hb (GHb). GHb results from post synthetic non-enzymatic modification of HbA. It is characterised by presence of glucose or glucose metabolite linked to amino terminal of beta chain of Hb molecule. The process involves irreversible post translation glycosylation of HbA within RBC, occurring continuously throughout its life span. Although methodological problems and difficulties in interpretation of results exist, the use of glycosylated haemoglobin (GHb) levels as an integrated index of long term blood glucose level is now accepted. Levels of GHb are believed to reflect the average blood glucose concentration over a period of 2-3 months and are

increased in diabetes. Its measurement shows better correlation to the degree of glycaemic control in management of diabetes mellitus than occasional periodic glucose estimation in blood or urine. This method of evaluating personnel especially aircrew coming for periodic review for Diabetes Mellitus or IGT (Impaired Glucose Tolerance) is very important. It has been noted at times, that surreptitious medication of oral hypoglycaemic agent are resorted to, prior to the board, so as to retain a higher medical category. In such cases, while isolated blood glucose estimation at the time of medical board may be normal, GHb levels may be a better indicator of long term glycaemic control.

Material and Methods

The study was undertaken in Dept of Aviation Pathology IAM IAF to measure the concentration of GHb in diabetics and those having IGT (Impaired Glucose Tolerance) and to correlate this with degree of glycaemic control based on blood glucose levels.

The study comprised of 48 male subjects drawn from Command Hospital, Air Force and those reporting to IAM for medical boards. 17 healthy young adults were also included in the study as controls. The average age of subjects varied from 28 years to 71 years. They were divided into those having frank diabetes (n=38) and IGT (n=10). The criteria for diagnosis of diabetes mellitus and IGT were as follows :

IGT—Fasting blood sugar > 100 but < 120 mg/dl
Post prandial blood > 120 but < 180 mg/dl
sugar

Diabetes Mellitus

Fasting BG	>	120 mg/dl
PP BG	>	180 mg/dl

The duration of diabetes/IGT varied from 3 months to 19 years. All the cases of diabetes belonged to Type II diabetes (non insulin dependents) Of the 38 cases of diabetes, 16 were on diet alone, 19 were on oral hypoglycaemic agents and 3 cases

were on insulin. The clinical assessment of diabetes was based on blood glucose levels and were divided into two groups :

- Fair control (n=20) with PP blood glucose less than 200 mg/dl.
- Poor control (n=18) with PP blood glucose more than 200 mg/dl.

Glycosylated Haemoglobin Estimation : Venous blood was processed for blood glucose and glycosylated Hb. Blood glucose was estimated by modified Folin WU's method and GHb by Fluckiger and Winterhalters method. The principle of the method was precipitation of proteins of haemolysate after hydrolysis with oxalic acid and reaction of supernatant with thiobarbituric acid to obtain yellow chromogen of furfural compound. This was measured at 443 nm in spectrophotometer. GHb was calculated on the assumption that 1% GHb corresponds to absorbance of 0.029 at 443 nm.

Results

GHb values obtained with varying degree of glycaemic controls are shown in Fig. 1.

- Normal healthy subjects :
5.18% (Range 3.97-6.23%)
± 0.65
- Impaired glucose tolerance :
5.49% (Range 4.63-6.31%)
± 0.46
- Diabetes fair control :
7.03% (Range 5.31-8.72%)
± 1.01
- Diabetes poor control :
9.49% (Range 6.84-13.37%)
± 1.57

A highly significant correlation (P 0.001) was found between GHb values and PPBG. The highest reading obtained in this study was 13.37 with PP blood glucose of 420 mg/dl. He was on antitubercular treatment also (known to give falsely elevated

figures). Two known cases of diabetes, were found to be taking hypoglycaemic agents, based on GHb reading. Both of these produced normal F and PPBG. GHb levels were found to be 8.4% and 8.7%. Subsequent GTT done on them showed diabetic response in both of them.

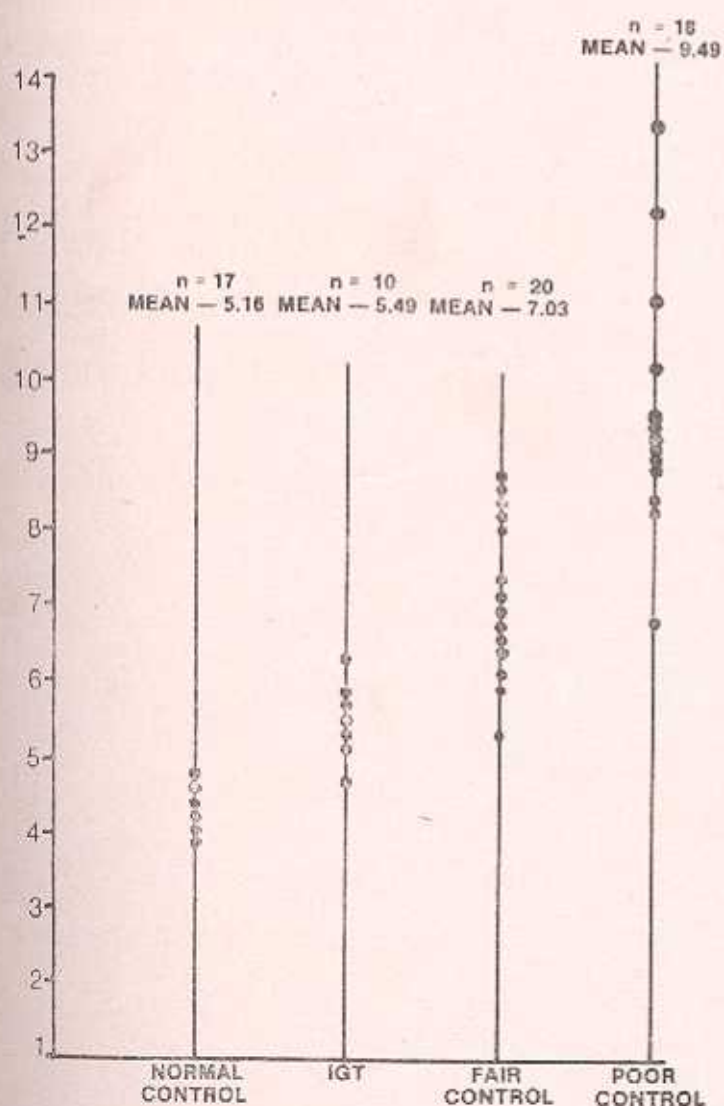


FIG - 1 LEVELS OF GHb WITH VARYING GLYCAEMIC CONTROL

Discussion

Proper assessment of glycaemic control is an essential part of management of diabetes mellitus. Occasional blood glucose estimation is given undue importance both by the patients and physicians. Service et al (1980) observed that variation in blood

glucose may be so great that isolated estimations are likely to give incomplete and often misleading impressions. Variation in diet, physical activity and patients' cooperation, seriously limit the value of isolated blood glucose estimations. Individual tends to fast or diet better, before the blood glucose estimation, thereby producing better blood glucose values. Similarly, they may resort to drugs just before medical boards for their benefit, as in two of our cases. Repeated blood glucose monitoring (done many times a day) provides a satisfactory index of assessment but has its obvious limitation.

The evolution of GHb as a test in diabetes, began in 1968, with demonstrated elevation of minor haemoglobin in diabetes. Bunn et al in 1976 pointed out that HbA1 is related to diabetes. It is an objective index, independent of patient cooperation and reduces the measurement to a single test once in 2-3 months. It is not affected by variation in renal threshold, changes in patients diet, relation to meals and deliberate medication. However, it gives no information about instant blood glucose value and is of no use in the management of acute complications. It gives unreliable information in anaemias, haemoglobinopathies and stress hyperglycaemia. Values of GHb noted in this study in healthy controls and diabetes are comparable to those reported by Jackson et al and Raheja et al. Some difference in values have been reported by various authors due to difference in methodology. Gonan et al found impressive correlation of GHb with BG while Nabbaro et al found the correlation to be not satisfactory. In this analysis, PPBG values showed statistically significant correlation with GHb ($p < 0.05$); clinical assessment with BG estimation also correlated well with BG.

Glycosylated haemoglobin was found to be within normal limits in IGT cases in this series, but as a group they showed significant elevation as compared to normal people. It might indicate that this group has increased glycosylation. This finding is in variance to Bennett et al (quoted by Chandalia et al) who showed absence of significant elevation of GHb in IGT cases. Although, study is small

(total cases 10), it strongly questions the WHO classification, where a patient with IGT is told that he does not have diabetes and left alone.

Conclusions and Recommendations

Measurement of GHb is a useful parameter for evaluation of long term glycaemic control or compliance to treatment in diabetes mellitus. Although, it gives no display of glucose value at the time of testing, it may possibly give information regarding stability of diabetic state, inspite of the variation of blood glucose levels due to diet, physical activity and tendency for surreptitious medication at the time of test. This has a special relevance to personnel of Armed Forces who may have asymptomatic diabetic status not brought out due to the laid down blood glucose criteria and also in the light of possible self medication. This is all the more important in aircrew - civil as well as military, who are handling highly sophisticated modern aircraft and in whom a proper evaluation is essential. As the test is technically simple and can be carried out in any hospital laboratory, which is equipped with a Spectrophotometer, its introduction as a routine test is recommended.

