GLYCOSYLATED HAEMOGLOBIN IN THE DIAGNOSIS OF DIABETES MELLITUS

Ramanakumar, T. K., Seshiah, V.*

Summary

Glycosylated Haemoglobin (GHb), the resultant of chronic hyperglycaemia, has hitherto been used as an index of long term glycaemic control in diabetics. Since it is a refiector of integrated long term glycaemic status, it can also be used as a screening test for the diagnosis of Diabetes Mellitus (DM). In this study of 1000 subjects, when GHb was compared to Oral Glucose Tolerance Test (OGTT) in the diagnosis of DM, GHb was found to have 93.98% sensitivity, 85.86% specificity and 93.14% efficiency in the diagnosis of DM. The predictive value of an elevated GHb is 98.2%. Hence it is concluded that GHb is a useful screening test for DM and that it may also be considered when criteria for the diagnosis of DM are discussed.

Introduction

Glycosylated Haemoglobin reflects retrospective time averaged glycaemic status of an individual and thus has became a useful tool in assessing the long term control of DM[1,2,3]. Being a reflector of chronic hyperglycaemia, an elevated GHb, can also be used as a screening test for the diagnosis of DM[4,5]. It has the added convenience that blood sample can be collected at any time of the day without any specific time interval in relation to the meal.

Materials and Methods

Glycosylated Haemoglobin was determined in 1000 non-pregnant adults attending the Dept. of Diabetology, Madras Medical College and Govt. General Hospital, Madras in whom 75G Oral Glucose Tolerance Test was done. The OGTT was interpreted following the WHO criteria[6]. Glycosylated Haemoglobin was estimated by modified Fluckinger and Winterhalter's method[7].

Results

The OGTT following WHO criteria, revealed that among the 1000 subjects studied, 797 had DM while 111 had Impaired Glucose Tolerance (IGT). The remaining 92 had normal glucose tolerance (Table-1).

The mean GHb in those with normal glucose tolerance, IGT and Diabetes Mellitus was 6.9 ± 1.05%, 8.4 ± 2.50% and 12.6 ± 1.80% respectively. Table 2 shows the 95% confidence limits of GHb in each of these categories. The +2SD figure for those with

*Dept. of Diabetology, Madras Medical College and Govt. General Hospital, Madras-600003.

Table 1

Results of OGTT

n = 1000

Diagnostic category (WHO)	Number	Percentage
DM	797	79.7
IGT	111	11.1
Normal	92	9.2

Table 2

GHb in different categories of Glucose Tolerance

n=1000

Categories of Glucose Tolerance	No. of subjects	GHb% Mean ± S.D.	GHb -2SD	GHb +2SD
Normal	92	6.9 ± 1.05	4.8	9:0*
IGT	111	8.4 ± 2.50	5.9	10.9
DM	797	12.6 ± 1.8	9.0*	16.2

*+2SD of GHb in those with normal glucose tolerance and
-2SD of GHb in. those with DM are both 9 %, including that a GHb level of 9% is the cut-off point between the. two categories.

those with normal glucose tolerance and the -2SD figure for those with DM are both 9%, indicating this to be a clear cut-off point between the normal-and diabetic population in this study. The mean GHb value in those with IGT lies between those of the other two two categories.

The GHb was elevated in 749 diabetics, 60 subjects with IGT and 13 subjects with normal glucose tolerance. It was normal in 48 diabetics, 51 subjects with IGT and 79 normal individuals.

Further analysis was restricted to those who had either normal glucose tolerance or DM.

Table 2 shows the GHb results in relation to the OGTT results in subjects who had either diabetic curve or normal glucose tolerance.

Analysis of Results

Oral Glucose Tolerance Test was taken as the reference "Gold Standard" against which the validity of GHb determination in the diagnosis of Diabetes Mellitus was assessed. Based on the OGTT and GHb results, subjects could be placed into one of the following 4 wells depicted in Fig. l. Thus,

Fig. I

Classification of subjected based on OGTT and GHb

		OGTT	
		Abnormal	Normal
GHb	Elevated	a	b
	Normal	c	d

Well "a" represents diabetics with elevated GHb

Well "b" represents normal subjects with elevated GHb

Well "c" represents diabetics with normal GHb, and

Well "d" represents normal subjects with normal GHb

In other words,

Well "a" represents True positivity

Well "b" represents False positivity

Well "c" represents False negativity

Well "d" represents True Negativity of GHb estimations in the diagnosis of DM in relation to OGTT

After so placing the results of GHb determination in relation to OGTT results, we proceeded to analyse the various attributes of GHb in the diagnosis of DM.

Sensitivity of GHb in the diagnosis of DM

The sensitivity of GHb in the diagnosis of DM, i.e. its ability to correctly identify those with DM as compared to OGTT is given by the formula :

$$\frac{a}{a+c} \times 100$$

Specificity of GHb in the diagnosis of DM

The specificity of GHb in the diagnosis of DM, i.e. its ability to correctly classify those who do not have Diabetes, as compared to OGTT is given by the formula :

$$\frac{d}{b+d} \times 100$$

Predictive Value of raised GHb in the Diagnosis of DM

The predictive value of raised GHb in the diagnosis of DM represents the percentage of diabetics among all those who have raised GHb and is given by the formula :

$$\frac{a}{a+c} \times 100$$

Predictive Value of normal GHb

By the predictive value of normal GHb is meant the percentage of true normals by OGTT among all those who have a normal GHb and this is given by the formula :

$$\frac{d}{c+d} \times 100$$

Efficiency of GHb as a diagnostic test for DM

Having analysed the sensitivity, specificity and predictive value of GHb in the diagnosis of DM, we proceeded to analyse its overall efficiency as a diagnostic test for DM. The efficiency of a test represents its ability to bisect the test subjects into either normals or abnormals-i.e: in this instance place them either into well `a' or well `d' and is given by the formula $\frac{a+d}{N} \times 100$ were N represents the total number of subjects tested.

Discussion

Various tests for the diagnosis of DM exist. Glycosuria depends on the renal threshold for glucose so much that it is less sensitive in diagnosing diabetes. Since DM can be present despite a normal fasting blood sugar, it is also less sensitive. Further even when it is elevated, National Diabetes Data Group (NDDG)a requires it to be elevated on more than one occasion to be diagnostic. Unequivocal elevation of random or postprandial blood sugars are also required to be demonstrated on more than one occasion. When all these tests are inconclusive and yet the diagnosis of DM is in doubt, an OGTT is recommended. All these blood sugar tests have the inconvenience of having to collect the blood sample at a specified time or preparing the patient. Glycosylated Haemoglobin determination which reflects integrated glycaemic status of about 2-3 months is a useful screening test for the diagnosis of DM by the very nature of its evolution, viz. duration and degree of

hyperglycaemia. In addition, it has the advantage that blood sample can be collected at any time without any specified time interval in relation to meal.

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