Significance of Glycosylated Haemoglobin (Hb) in Diabetic Patients

Dr. Dipesh Prajapati [1], Dr. Vaishali H Anand [2], Dr. Mahesh Patel[3]

Abstract

In normal, non-diabetic control group subjects, mean glycosylated haemoglobin concentration is 6.68% and range is 5.02 to 7.93.In present study mean glycosylated haemoglobin concentration is 12.90. Glycosylated haemoglobin correlates significantly with the fasting, post prandial levels. Mean of fasting and post –prandial blood sugar level are 178.68 and 226.28 mg /dl respectively. Glycosylated haemoglobin value found higher in female -13.01 compare to make -12.86 Glycosylated haemoglobin values were higher in Juvenile onset diabetes (IDDM) – 14, 20 than Maturity onset diabetes (NIDDM) 12.26. A Glycosylated haemoglobin value has no relation with the long complication of diabetes mellitus. Glycosylated haemoglobin concentration was found high in Insulin taking 15.26 than patients on oral hypoglycaemic agents 12.25 and on dietary restriction 7.81. Single Haemoglobin A1c measurement reflects the mean blood sugar concentration of the patient for the previous two to three months. Therefore, the glycosylated haemoglobin assay provides information about the degree of long term glucose control that is otherwise obtainable in the usual out patients setting. ION EXCHANGE RESIN method can be used routinely to estimate HbA1c in non-diabetic and diabetic patients. Periodic monitoring of HbA 1c should allow the assessment of chronic diabetic control on an out patients basis in a more objective manner than is now possible and enable one to evaluate various forms of therapy and the relationship between carbohydrate control and the progression of various diabetic sequele.

Keywords: Diabetes Mellitus, Glycosylated Haemoglobin (HbA1c), Insulin

[1] Consultant Pathologist, [2] Assistant Professor, Pathology, [3]Associate Professor, Pathology, B.J. Medical College, Ahmedabad, Gujarat (India)

Corresponding author mail: andvaishu@gmail.com

Introduction

Diabetes mellitus (DM) is now one of the most common non-communicable diseases globally. DM is a chronic metabolic disorder characterized by hyperglycaemia, either because the body does not produce

enough insulin, or because cells do not respond to the insulin that is produced. The worldwide prevalence of diabetes in 2000 was approximately 2.8% and is estimated to grow to 4.4% by 2030.[1] Magnitude of DM in Bangladesh is also increasing day by day. Prevalence of DM in our country is about 6.1% (5.6 millions) and it will hold the 8th position in the world according to the total cases of diabetes in adult population (20 to 79 years) by the year 2030.[2,3]

The HbA1c assay has become the most commonly used measure of chronic glycaemia in epidemiological studies, clinical trials and the management of diabetes since its introduction more than 25 years ago[4].

HbA1c was introduced into clinical use in the 1980s and subsequently has become a cornerstone of clinical practice[5].

HbA1c reflects average plasma glucose over the previous eight to 12 weeks[6]. It can be performed at any time of the day and does not require any special preparation such as fasting. These properties have made it the preferred test for assessing glycaemic control in people with diabetes. More recently, there has been substantial interest in using it as a diagnostic test for diabetes and as a screening test for persons at high risk of diabetes[7]. Over the last four decades HbA1c comes out with many facts of diabetes and now it is a very important part of both diagnosis and treatment of diabetes. However, HbA1c may be affected by a variety of genetic, physiological, haematological and illness-related factors but another major factor concerns costs and availability of HbA1c assays in many countries. Thus we investigated significance of Glycosylated Hb in Diabetic Patients

Materials and Method

This study was carried by measuring Glycosylated haemoglobin using cation exchange resin method at our referral teaching hospital in Ahmadabad from January 2007 to October 2008. Measurement of total HbA1c and blood sugar were carried out at "Diabetic research lab" at BJMC Ahmedabad.

We included 40 non diabetic and 90 diabetic patients, out of which 60 were having NIDDM and 30 was having IDDM.

All patients were selected from the cases who were admitted in civil hospital or attending diabetic clinics as outdoor patients.

In all cases Glycosylated Haemoglobin measurement along with other necessary investigation was done on same day.

Observation and Results:

In this study there are 40 Non – diabetic control subjects and 90 diabetic patients were studied. In study group of 90 diabetic patients there are TYPE –I, TYPE –II, Newly diagnosed as well as established cases, well controlled and poorly controlled, with complications and without complication. Throughout this study, results of different parameters are expressed by using these groups.

Table -1: Control group (Group =A)

GROUP (A)	NO.	%	FBS (mean)	PPBS (mean)	GHB (mean)
T	40	100 %	83.72	103.02	6.68
M	24	60 %	84.01	101.96	6.77
F	16	40%	83.31	104.62	6.54

Control group includes 40 Non- Diabetic normal subjects. Out of these 40 normal subjects, 24 were male and 16 were females, mean age of them was 37.95 years. (Range: 18-70 years).

Mean HbA 1 c value in this group is 6.68. Range is 5.02 to 7.93

STUDY GROUP (Y +Z): This include all 90 diabetic patients and of these 60 were Male and 30 were Females. Mean age of them was 44.53 (Range -18-72 years)

TABLE -2: CASE GROUP

GROUP	Gm Hb %	
	MEAN ± SD	RANGE
Y	9087 +-1.04	7.58 to 13.99
Z	13.92 +-1.84	10.43 to 18.98

This includes all 90 diabetic patients and of these 60 was male and 30 were females. Mean age of them was 44.53 (Range – 18.72 years.)

In this group two sub-groups were identified.

GROUP Y: (Well controlled diabetic): Defined as blood sugar in non –diabetic range: FBS< 120 mg/100 ml, PPBS<180 mg/100 ml

In this 23 patients included, and out of this 15 were male and 8 were female.

GROUP Z: (Poorly controlled diabetic): Defined as blood sugar in diabetic range: FBS >120 mg /100ml & PPBS>180mg/ 100 ml

In this 67 patients included, and out of this 45 were male and 22 were female

All those patients, who had duration of diabetes within three months from the day of measurement were considered “newly detected" diabetic patients and rest of the patients were considered "old case" or “established case". There were 12 newly detected and 78 old cases of diabetic in this study using above criteria. In the study group (y+z) there is mean HbA 1c value is 12.90 lowest being 7.51 (case No.98). Highest being 18.98 (case No. : 48).The mean value is almost being two times higher than that control group.

Age Distribution: In case group mean age is 44.53% years and in this group the maximum number of patients in 41 to 50 year age group. The minimum age being 18 years and maximum age being 73 years.

Weight Wise and Sex Wise Distribution: In study, the mean weight is 64.89 kg, in men mean weight is 65.08 kg and in female 63.98 kg. Mean weight is higher in male than female.

There are 10 overweight or obese patients in this study group (Average weight 95 Kg)

Obese patients show significantly higher GHb levels. Mean GHb level is 15.10 %

In this study mean GHb level of female is 13.01 % which is more than GHb level of males 12.64.

Type of Diabetes Mellitus: In control group mean GHb of male is 6.77 & female 6.54, in study group mean GHb level is 12.90 %, in male 12.84%, in female 13.01 %.

In IDDM male have mean GHb is 13.82 and in female 14.96, mean is 14.43. In NIDDM mean GHb is 12.20, male have GHb level 12.80 and female have 12.51, having higher value in female than in male.

In clinical diagnosis of Type 1 (IDDM) verses Type 2 (NIDDM) diabetes mellitus was established at the time of measurement of GHb according the following criteria.

- Age of the onset of diabetes
- Rapid or slow onset
- History of significant ketonuria and /or body weigh

In IDDM, the mean GHb : 14.43% , mean age :28 years (Range18-43), In NIDDM the mean GHb :12.20% , mean age : 51 years (Range 30-72), Thus, in IDDM there is higher value of mean GHb 14.43%, then in NIDDM mean GHb value 12.20%

Duration of Diabetes Mellitus: In study group as the duration of DM is increasing, the level of GHb also increases steadily as shown in table 3. Out of 90 diabetic patients, family history of diabetes is positive in 20 patients, out of these 9 are of NIDDM, 11 of IDDM.

Table-3: Duration of Diabetes Mellitus

GROUP	NO	%	gmHb(mean)
CASE	90	100%	12.90
0-5 yrs	50	55	12.79
5-10 yrs	22	25	13.01
>10 yrs	18	20	13.18

There is no significant difference in patients with complication (12.66%), and patients without complication (12.98%)

Patients having Insulin therapy have higher value (15.26) then with on Oral hypoglycaemic agents (12.25) and patients on dietary modification had level value (7.81). Table 4 shows correlation of various parameters with Hb A1c

Table-4: Various Parameters of Diabetes Control and HbA1c

GROUP	NO.	FBS (mean)	PPBS (mean)	GHb (mean)
CONTROL	40	83.72	103.02	6.68
STUDY	90	178.68	226.52	12.90
IDDM	28	166.33	221.48	14.43
NIDDM	62	193.89	251.32	12.20

Value comparison in various diabetic group in present study.

Mean value of all three variables are significantly greater in diabetic group than in non- diabetic group. HBA 1c, FBS, PPBS value for each plotted in graph I. There is slight overlap of HBA 1c in diabetic and non- diabetic patients, but marked overlap in FBS and PPBS in diabetic and non-diabetic patients.

Findings clearly indicates that association between FBS, PPBS one and HBA 1c is positive to a high degree (r = 0.74,0.62) which shows levels of GmHb are directly proportional to the levels of FBS & PPBS and this coefficient of each parameter is highly significant p>0.001.

Discussion

The goal of prevention of longterm diabetic complication may be achieved by chronic glycemic control in diabet6ic patients. To obtain this goal, proper assessment of glycemic control becomes an essential part of management. Determination of Glycosylated haemoglobin is new and unique method of measuring the level of chronic glucose control in diabetic patients.

This study was conducted on Control Group (X) of 40 non- diabetic persons and Study Group (Y + Z) of 90 diabetic patients to find our relation of glucosylated haemoglobbin and different aspects of diabetes mellitus. In this study various aspects of diabetes like control, complications and effect on levels of Glycosylated haemoglobin is studied and levels of GHb measured by Ion exchange resin method.

In diabetic patients (n=90) mean HbA 1c value is 12.90% and range: mean +-SD: 12.90+-2.52 So, (7.51 to 18.98), is also accordance with the previous study by Abraham E.C[8].

TABLE 4 Also show that if hyperglycemia is increased then HbA1c value also increase correspondingly and improvement in glycemic control reduce HbA1c values proportionately. Gone B. et al[9] and other have reported the similar results. These results in present study in present study are comparable to their study.

Table 5 shows that HbA1c reveals correlated significantly with fasting blood sugar in both diabetic groups. Similarly in study of S. Khullar[10] correlated highly and significantly in non- diabetic and diabetic groups.

Table 5: Correlation of HbA1c with FBS in Various Sub-Groups and Its Correlation with Previous Study of S. Khullar[10]

GROUP	PREVIOUS STUDY		PRESENT STUDY	
	"r"	"p"	"r"	"p"
X	0.78	>0.001	0.62	>0.001
Y	0.94	<0.001	0.85	<0.001
Z	0.63	<0.02	0.90	<0.001

Table 6: Correlation of HbA1c Values with FBS in Different Sub-Groups and its Correlation with Previous Study of S. Khullar[10]

GROUP	PREVIOUS STUDY		PRESENT STUDY	
	"r"	"p"	"r"	"p"
X	0.80	>0.001	0.68	>0.001
Y	0.88	<0.001	0.82	<0.001
Z	0.79	<0.001	0.84	<0.001

Table 6 shows highly positive correlation between HbA 1c and PPBS level in both diabetic group and highly significant ($p<0.001$) and this results of present series also consistent with previous study of S. Khullar [10].

These findings suggest that HbA 1c values do not reflect glycemic value in normal subjects in our present series. One of the explanations may be that normal subjects in the present series are having very narrow range of blood sugar value, but relatively wide range of HbA1c value. Thus narrow rnge and restricted value of blood sugar might have affected this correlation ship.

HbA1c determination may provide an alternative method of screening for diabetes. This if an attractive concept because of HbA 1c level can be measured from a single blood sample taken at any time of day without prior dietary preparation and yet provide highly representative measure of the average blood glucose concentrations[11]. Oral glucose tolerance test has poor reproducibility and results are affected by various factors. Moreover, it is non-physiological test in nature. The load of 75 grams glucose is not encountered in day to day life[10]. Thus the oral glucose tolerance tests, although a very sensitive test to diagnose patients with diabetes mellitus has low specificity. In contrast the HbA 1c det4ermiantion has low sensitivity but high specificity[11]. The sensitivity if test directly related to the quality of determination. This aspect of HbA 1c assay is studied in present series as follows:

Even when 99.7% confidence limit is taken for normal range, there is overlap of HbA 1c levels in 2 cases of control and diabetes, so it can be reduced that subjects with HbA 1c value less than 9.08% are likely to be non – diabetics. So, cut of point of 9.08% of HbA 1c levels for normal and diabetics is suggested. These findings in present series confirms the

results of previous study done by S. Khullar[10] that HbA1c can be used as screening procedure for detection of diabetics.

Table 7: Hba1c Values in Different Sub-Groups and Its Correlation with Previous Study of S. Khullar[10]

GROUP	PREVIOUS STUDY		PRESENT STUDY	
	MEAN +-SD	RANGE	MEAN +-SD	RANGE
X	6.39+-0.85	4.78 to 8.20	6.69 +-0.78	5.02 to 7.93
Y	13.06+-1.80	10.20+-18.16	13.92+-1.84	10.43 to 18.98
Z	9.20+-1.02	7.84+-10.48	9.87+-1.04	7.58 to13.79
Statistics	Previous study		Present study	
x:y	P>0.001		P >0.001	
y :z	P>0.001		P>0.001	

Table 7 shows that HbA 1c values in control are in the range of 5.02 to 7.93% (6.68+-0.78%) taking 99.7% confidence limit (i.e. 3 S.D.). the normal range of HbA1c will be 4.40 to 9.08%(Mean+-3 S.D.). So 99.7% of normal non-diabetic population will have HbA 1c levels in this range. HbA1c level in group "Z" i.e. diabetics patients with poor control (i.e. blood sugar in diabetic range) is 13.92+-1.84(range 10.34% to 18.98%) and this is highly significant than the values in control group in present study.

Glycosylated haemoglobin assay is superior of the traditional blood sugar values in discriminating diabetic from non-diabetic patients. There is overlap of the diabetic and non diabetic HbA 1c value in 2 cases (2.22%) out of 90 patients. Such an overlap in FBS value is also found in 18 cases (20%) Out of 90 patients, for post-parandian blood sugar values such overlap is present in 5 out of 90 patients (5.55%).These findings are consistent with generally accepted mechanism of formation of glycosylated haemoglobin, that it is an integral related to the average blood sugar level to which the haemoglobin is exposed.

Consequently this should provide a better discriminate of diabetic from the non-diabetic than a rapidly fluctuating variable like blood sugar values.

Conclusion

In diabetic patients Glycosylated haemoglobin concentration is two to three folds higher than that in normal subjects.

In present study mean glycosylated haemoglobin concentration is 12.90

Glycosylated haemoglobin correlates significantly with the fasting, post–prandial levels. Mean of fasting and post–prandial blood sugar (PPBS) level are 178.68mg/dl and 226.28 mg /dl respectively.

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Glycosylated haemoglobin assay provides better discriminations of diabetic form the non-diabetic than a rapidly fluctuating variable like blood sugar. Discrepancy between the results of glycosylated haemoglobin and clinical impression of control of results of blood sugar of patients, can give an indication to treating physician to look back into details history and modify the therapeutic regimen accordingly.

Glycosylated haemoglobin assay defines an end point as the foal of diabetic therapy. The least results can provide a powerful stimulus to the patients to improve their compliance.

Glycosylated haemoglobin assay may provide an alternative method of screening for diabetes.

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