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Research Article

Glycosylated Hemoglobin In Cases Of Diabetes Mellitus With Microangiopathy

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ABSTRACT

Objective: To analyze glycosylated haemoglobin in patient of diabetes with microangiopathy. Method: Study done on 100 patients out of which 80 are well known case of diabetes out of which 50 are diabetes with micro-angiopathy and rest 30 are diabetes without micro-angiopathy and other 20 are non-diabetes considered as normal healthy control. Result: Out of 50 cases of diabetes with micro-angiopathy 15 cases having retinopathy in which 67% males and 33% Females and the mean glycosylated Hb level is 10.89% at beginning and 8.86% after 3 months; 19 cases having retinopathy with nephropathy in which 63% were males and 37% were females the mean glycosylated Hb is 12.73% at beginning and 10.52% after 3 months whereas 16 cases having nephropathy in which sex distribution was 63% males and 7% females and the mean glycosylated Hb is 11.76% at beginning and 8.39% after 3 month. Conclusion: The three months follow up study showed a significant fail in HbA1C level in all groups of diabetes with and without microangiopathy. But it does not touch to normal level 4.7% of total Hb. Assessing Glycaemic control in diabetes with high glycosylated haemoglobin levels, concurrent fasting blood glucose level estimations are essential.

INTRODUCTION

Diabetes mellitus is considered as a chronic metabolic syndrome with persistent hyperglycemia which is occurs either with insulin deficiency or resistant. According to the IDF (International Diabetes Federation), worldwide approx. 537 million adults of age between 20 to 79 years are with diabetes, which is estimated that till 2030 total number of people with diabetes is projected to rise to 643 million and 783 by 2045 whereas in South-East Asia 90 million people are with diabetes till 2021 which is estimated to be 113 million by 2030 and 152 million by 2045.[1]Glycation of Hb is a physiological process, in healthy adult RBCs contains HbA – 97%, HbA2 – 2 – 2.5% and HbF – 0.5%, out of that HbA1 is approx. 6% of total. On the basis of electrophoretic properties HbA1 are separated into four fractions

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HbA1a1, HbA1a2, HbA1b and HbA1c whereas HbA1c is prominent fractions which comprises 5% of total HbA.[2]By Rahbar S, et al. reported in 1969 that diabetes mellitus patients with increased HbA1c.[3] In 1975, Bunn HF, et al identified the pathway leading to the formation of HbA1c.[4]The use of HbA1c as a biomarker to monitor blood glucose levels among diabetic patient where proposed by Koenig RJ, et al in later 1976.[5]Detecting glycosylated HbA1c levels not only importance in diagnostic but also for assessing diabetes mellitus managements. HbA1c was not included as a diagnostic tool till 2011 but by World Health Organization in 2011 considered it as biomarker in diagnosis of diabetes mellitus along with International Expert Committee and American Diabetic Association, in 2009 and 2010 respectively.[6]

The pathological manifestation of microangiopathy in diabetes includes the disorders in nerve tissue, retina, myocardium and kidney.[7] The widely used golden standard for diabetes control is glycosylated haemoglobin (HbA1c) levels in the clinics.[8] The blood glucose level for the longer times is in a high level in the patient with diabetes microvascular diseases lead to cause chronic injury and dysfunction of many tissues.[9]So, this study was done to evaluate the clinical significance of glycosylated haemoglobin (HbA1c) in the assessment of metabolic control in diabetes mellitus with microangiopathy.

MATERIAL & METHODS

The study was carried out in the Department of Biochemistry at Shri Krishna Medical College, Muzaffarpur, Bihar and nearby private clinics and labs on newly diagnosed cases of diabetes (fasting glucose >126mg/dl,post prandial>200mg/dl & HbA1c >6%).Glycosylated haemoglobin estimation was done by latex turbidimetric method via human kit supplied by Bio-line Diagnostics.

Selection of Patients: -

The total 100 patients were included in the study out of that 80 well known cases of diabetic were selected random, comprised of both sex ranging from 20yrs to 80yrs age. The duration of diabetics in the patient varied from 1 month to 21 years before the time of detection. Out of that 30 cases are diabetes without evidence of micro-angiopathy and the rest 50 cases are diabetes with micro-angiopathy (retinopathy, nephropathy, and neuropathy). The other 20 cases are non- diabetic which considered as a control group varied from 20 years to 80 years of age. They were also screened for diseases like haemolytic level; such were not included in the control group.

Examination: -

In the group of the examination of all these patients (case and control) following:

All the patients (case and control) were examined, and history were taken under the following heading of the case history performa: -

Name, Age, Sex, Weight, Religion, Address, Occupation, Chief complains, Detail Clinic History,Past Medical History, Family History, General Examination & Systemic Examination.

In general examination, more stress was given on pulse rate and changes after valsalvamaneuver, B.P. in lying down and standing position.

Retinopathy was detected by direct ophthalmoscopy examination of fundus with pupil dilated. The worsening of complications in this study was defined as an increase of one or more steps in the 4 stages of the modified ETDRS (Early Treatment Diabetic Retinopathy Study) interim scale for retinopathy.

Classification of Diabetic Retinopathy: (ETDRS Classification)[10]

ETDRS- Early Treatment Diabetic Retinopathy Study: -

Non- proliferative Diabetic Retinopathy (NPDR):-

A. Mild NPDR
- Atleast 1 microaneurysm (MA)

B. Moderate NPDR

- Hard exudates, venues beading arid intra retinal microvanecularabnormmalineb (RMA) definitely present.

C. Severe NPDR

- Haemoglobin/microaneurisms in all four quadrants of retina.
- Venous beading in 2 or more quadrants.
- IRMA in atleast 1 quadrants.

D. Very Severe NPDR

- Any 2 or more of C

RESULTS

The present study was carried out in 100 cases. Out of this, 20 healthy non-diabetics, 30 cases of diabetes mellitus without microangiopathy and 50 cases of diabetes mellitus with microangiopathy.

The patients group made for this study are as follows:

(1) Normal healthy control: This group was having 20 total patients. Out of that 12 (6%) male and 8 (40%) female.

(2) Patients of diabetes without microangiopathy: This group was consisting 30 patients with equal sex distribution i.e. 15 (50%) male and 15 (50%) females.

(3) Diabetic with microangiopathy.

(a) Retinopathy: This group was having 15 Cases with 10 (67%) males and 5 (33%) Females.

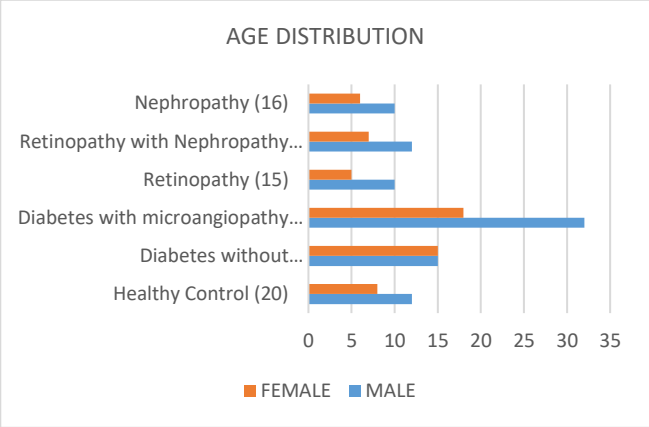
(b) Retinopathy with Nephropathy and Neuropathy: in this group also there were male predominance i.e out of 19 cases 12 (63%) were males and 7 (37%) were females.

(c) Nephropathy group was having 16 cases in which sex distribution was 10(63%) males and 6 (7%) females.

Table 1: Male – Female Ratio In A Groups

GROUP	MALE	FEMALE
Healthy Control (20)	12	8
Diabetes without microangiopathy (30)	15	15
Diabetes with microangiopathy (50)	32	18
Retinopathy (15)	10	5
Retinopathy with Nephropathy and Neuropathy (19)	12	7
Nephropathy (16)	10	6

Graph 1: Age Distribution



Incidence Rate:

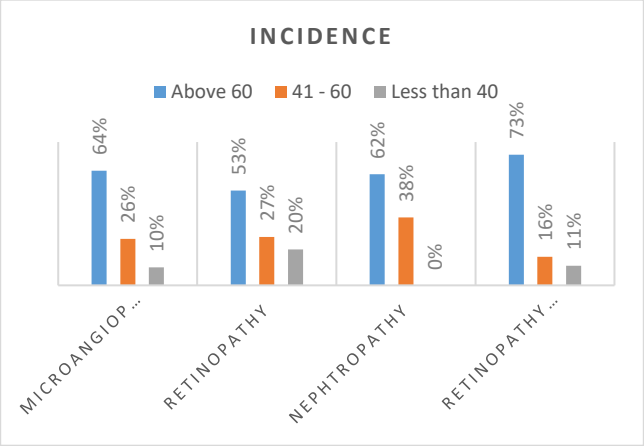
The incidence of microangiopathy is more 32 (64%) in the age group above 60 years, than other groups like 13(26%) in the age group 41-60 years and 5 (10%) in the age group less than 40 years. The incidence of Retinopathy is 8 (53%) in the age group more than 60 years, 4 (27%) in the age group 41-60 years and 3 (20%) in age group less than 40 years. The incidence of combined microangiopathy i.e Retinopathy with nephropathy and neuropathy is 14 (73%) in age group more than 60 years, 3(16%) in age 41-60 years and 2(11%) in the age group less 40 years. The incidence of Nephropathy is 10 (62%) in the age group more than 60 years, 6 (38%) in the age group 41-60 years and 0 (0%) in the group less than 40 years. The above data shows that incidence of combined microangiopathy i.e Retinopathy with Nephropathy and Neuropathy is more than isolated microangiopathy.

Table 2: Incidence Rate

AGE (Year)	Above 60	41- 60	Less than 40
Microangiopathy	64%	26%	10%
Retinopathy	53%	27%	20%
Nephtropathy	62%	38%	0%

Retinopathy with nephropathy and neuropathy	73%	16%	11%

Graph 2: Incidence Rate



Glycosylated Hemoglobin (HbA1C):

In control group, the mean glycosylated Hb level at beginning is 5.12 and after 3 month, 4.8 % there is no marked difference between this two values.

In diabetes mellitus without microangiopathy, the mean glycosylated Hb is 8.5% at beginning and 7.57% after 3 months of treatment.

In Retinopathy group, the mean glycosylated Hb is 10.89% at beginning and 8.86% after 3 months. In diabetics with combined microangiopathy i.e. Retinopathy with Nephropathy and Neuropathy the mean glycosylated Hb is 12.73% at beginning and 10.52% after 3 months.

In Nephropathy group, the mean glycosylated Hb is 11.76% at beginning and 8.39% after 3 month.

In this study we found that HbA_1C levels in all three groups of diabetes with microangiopathy category were on higher side than those of diabetes without microangiopathy. It is always more than normal healthy individuals. This reflects the view that HbA_1C level may be better indicator than blood sugar levels is assessing the severity of the disease.

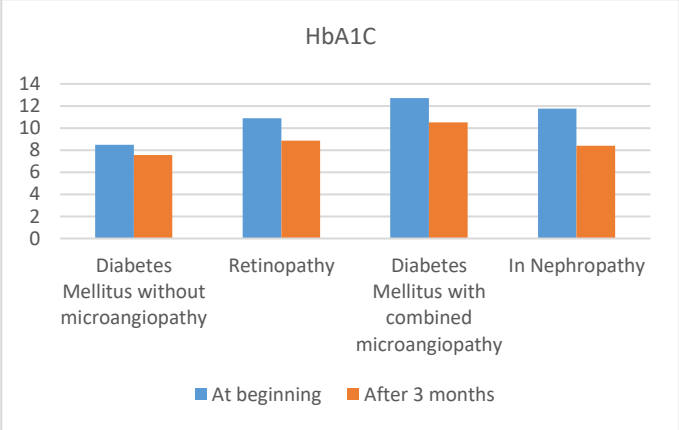
The blood sugar levels are indicative of one time values. While HbA_1C reflects a time bound value of approximately 8-12 weeks. A large study may be of proven HbA_1C value in two category i.e. diabetes with microangiopathy and without microangiopathy.

HbA_1C level reflects the averages blood glucose level during the previous 8-12 weeks, hence may fail in giving an accurate evaluation of blood glucose control throughout the entire duration of the disease.

Table 3: Glycosylated Hb (Hba1c) Level

HbA1C Level	At beginning	After 3 months
Diabetes Mellitus without microangiopathy	8.5	7.57
Retinopathy	10.89	8.86
Diabetes Mellitus with combined microangiopathy	12.73	10.52
In Nephropathy	11.76	8.39

Graph 3: Glycosylated Hb (HbA1C) LEVELS



Fasting Glucose:

The mean fasting blood glucose level in normal healthy individual varies from 70 mg % to 120 mg% among 20 persons. The corresponding glycosylated Hb varies from 4% to 6.5%. The mean fasting blood glucose level is 92.35 mg% and glycosylated Hb level is 5.12.

The fasting blood glucose level in diabetes mellitus without microangiopathy varies from 135 mg % and 255 mg %. The corresponding glycosylated Hb level varies from 6.5 to 10.4 %. Mean fasting blood glucose value is 197.2% and glycosylated Hb is 8.5%.

The fasting blood glucose level of Retinopathy cases varies from 236 mg % to 302 mg % mean is

266.93 mg %. The corresponding glycosylated Hb level is 9.6% to 21.1%. The mean is 10.89%.

The fasting blood glucose level in diabetes with combined microangiopathy varies from 270mg % to 378 mg %. The mean is 322.1 mg %. The corresponding HbA_1Clevel is 11 % to 14.6%. The mean is 12.73%. The fasting blood glucose in nephropathy cases varies from 240 mg% to 315 mg%. The mean is 289.81 mg %. The corresponding glycosylated Hb level is 10.1% to 12.5 %. The mean is 11.76%. These findings show that fasting blood glucose and glycosylated Hb level is more in diabetes with microangiopathy cases than normal individuals.

DISCUSSION

In the recent years, with the rapid social and economic development in India the living standard of people have been significantly improved along that the diet structure have greatly changes. At present still there is no cure for diabetes but which ever treatment present till date is mainly based on controlling the blood glucose level in order to reduce the complication of diabetes. With diabetes complication generally arises like microangiopathy, retinopathy, nephropathy, neuropathy and many more. Micro thrombus, thickening of capillary basement membrane and vascular proliferation are the common characteristics of diabetes microangiopathy.[11]

Diabetic with microangiopathy causes serious damage to the patients on multiple organs, which ultimately reduces the quality of life. Therefore, diabetes with microangiopathy are not only need to be early diagnosed but also should be treated which ultimately improve the quality of the life and also reduces the mortality and disability of the patient.[12]The clinical manifestation of microangiopathy disorders are not significant which lead to delay in diagnosis causing many systemic complications which landed up to the poor prognosis. Therefor the implementation of effective diagnostic and prediction method of microangiopathy are important.[13]

The blood glucose level (fasting and post-prandial) at the beginning of study and after 3 months treatment. It also shows the corresponding HbA_1C level at the beginning of study and after three months of treatment. This observation shows that three is excellent relation in fasting blood glucose level and HbA_1C level in both category i.e, diabetes with microangiopathy or without microangiopathy. In this study we find that blood glucose level declines sharply after treatment, but HbA_1C does not fall such rapidly.

This study also show that duration of diabetes was more prolonged in cases of microangiopathy as compared to the duration in group of diabetes without microangiopathy. It also shows that mean HbA_1C level which indicates that there is no significant correlation between duration of diabetes and HbA_1C concentration.

The comparison of mean fasting blood sugar in beginning of study of normal, diabetes mellitus without microangiopathy and diabetes mellitus with microangiopathy. This study shows that mean fasting blood sugar of diabetes mellitus without microangiopathy and diabetes mellitus with micropathy is higher than normal people.The comparison of mean glycosylated haemoglobin of normal, diabetes mellitus without microangopathy and diabetes mellitus with microangiopathy is highly significant. HbA_1C can accurately diagnose microangiopathy and it also play an important role in treatment and prognosis assessment. HbA_1Csynthesis process is relatively slower and cannot be reversed along that it also accurately reflect the blood sugar level over the past six to eight weeks.[14, 15, 16]

In the diagnosis and treatment planning HbA_1Cshould be considered as an important reference data because fasting blood glucose can be easily effected by outside factors including the diet pattern and sugar metabolism.[17]Even though

in our study, we found that diabetic patient with microangopathy had significantly higher $HbA_1C$and fasting glucose levels than those without. It also noted that HbA_1Cclearly shows the changes and has highly sensitive which can be help as a reference date for the clinician in diagnosis, treatment and prognosis of diabetic microangiopathy.

CONCLUSION

1. The three months follow up study showed a significant fail in HbA_1C level in all groups of diabetes with and without microangiopathy. But it does not touch to normal level 4.7% of total Hb.
2. HbA_1C level reflects average blood glucose concentrations of previous two to three months in diabetes with or without microangiopathy.
3. Microangiopathy does not hamper to decline of HbA_1C levels and attainment of good metabolic control.
4. HbA1c level does not fluctuate in relation to diet, exercise and anti-diabetic treatment on the day of testing.
5. Assessing Glycaemic control in diabetes with high glycosylated haemoglobin levels, concurrent fasting blood glucose level estimations are essential.

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