

The Ratios of Glycosylated Haemoglobin to Mean plasma glucose in Diabetes Mellitus Type -2 patients in predicting the early complications of the disease

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ABSTRACT

Background and Aim: The Measurement of hemoglobin A1c (HbA1c) is considered the gold standard for monitoring chronic glycemia of diabetes patients. There some studies of importance in monitoring glycemia which had showed events to established a direct relationship between mean blood glucose (MBG) and the development and progression of chronic diabetic complications.

Materials and Methods: 50 samples of non-Diabetic were taken as healthy controls and 50 samples of Diabetic patients of ages ranging from 35-80 years were studied by assessment of Glycosylated Haemoglobin and calculation of Mean plasma glucose were accounted for documentation in the study. The study was conducted in Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Hospital Central Lab for which the samples were analysed, sent from OP and IP of various dept in the hospital from September 2018 to February 2019.

Results: The mean, SD of Glycosylated Haemoglobin in controls (non -Diabetic) and subjects in the study group with Diabetes type-2 with long duration are shown in table-1 and 2 as 4.76 ± 0.62 in non -Diabetic controls and 8.44 ± 2.07 in Diabetic patients for GHB and It has been shown as 89.40 ± 24.90 in non-diabetic controls and 223.02 ± 73.80 in Diabetic patients for MPG . The ratios of GHB & MPG were shown in figure-2 as 18.78 for non-Diabetic and 26.42 in Diabetic patients respectively showing mean of subjects of diabetic patients increase than non- diabetic. The P values showed highly significant less than 0.0001 and for ratios which were calculated was less than 0.0014.

Conclusion: The Glycosylated Albumin [GA]/GHbA1C ratio was unpredictable but the ratio of GHbA1C/ Mean plasma glucose showed that it is better parameter to use in clinical practice in the present study for the containment of complications in Diabetic patients due to easy to interpretation and as there is correlation between GHB and Mean plasma Glucose.

Keywords: Ratios of GHbA1C, Mean plasma glucose in diabetic patients

INTRODUCTION

The HBA1C is most commonly needed test for the patients with diabetes mellitus type 1 and 2. The estimation of HBA1C is the gold standard for monitoring glycemic index of these patients. Its levels indicates the plasma glucose levels of previous 3 months status, as it is well known that long term chronic diabetic mellitus leads to serious complications to combat it in further course of time, which may lead to increased morbidity and mortality. However, it is in dreaded condition until the

serious complications are exposed by then it is not known to the patients. Therefore, it is prudent to estimate the HBA1C at regular intervals for its monitoring the glycemic status and plasma glucose levels which helps in management of diabetes and its complications at early possible course of the disease.

History of HBA1C date backs to 1958, when Huisman and Meyering first used chromatographic technique to separate HAB1C to the other forms of hemoglobins.^[1] Since then in 1975 more researchers were interested in

moderation of latest methods in estimation of it. The HPLC method proves the best for HbA1C levels to be predicted. [2]

Hence the monitoring of it is the best method to follow, as it shows better relationship to mean plasma glucose and progression of complications occurring [3], In spite of those conditions, which cannot be possible for estimation like hemolytic anemia and renal failure. [4]

Therefore, the present study on ratios of GHB to Mean glucose levels is taken up to infer the status of diabetes leading to adverse complications, which can be prevented by the prediction of ratios as there are many impacts and static influences of these parameters in their measurements in diagnosing the diabetic patients.

MATERIALS AND METHODS

50 samples of non-Diabetic were taken from healthy controls and 50 samples of Diabetic patients of ages ranging from 35 -80 years were studied by assessment of Glycosylated Haemoglobin and calculation of Mean plasma glucose were accounted for documentation in the study after standard procedure for taking consent.

The study was conducted in Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Hospital Central Lab for which the samples were analysed, sent from OP and IP from various dept in the hospital from September 2018 to february 2019.

The blood Samples were procured with precaution and use of standard methods for collection were analysed in Fine care analyser by using Fluorescence immunoassay quantitative rapid kit for Glycosylated Haemoglobin values and Mean plasma Glucose by calculation using the formula $MPG = [35.6 \times HbA1c] - 77.3$ [Rohling CL etal]. The levels were interpreted for GHB & Mean plasma Glucose and documented results were assessed by student 't' test to obtain statistical significance.

Inclusion Criteria

Prolonged diabetic history with no complication and no occurrences of any other systemic disorders.

Exclusion Criteria

Pre-diabetic, pregnancy, Hypertensive and Renal disorder patients were excluded in this study. The ratios of GHB to Mean plasma glucose were calculated and statistical significance was assessed.

RESULTS

The mean, SD of Glycosylated Haemoglobin in controls (non-Diabetic) and subjects in the study group with Diabetes type -2 patients, which are shown in table-1 and 2.

Table 1: The mean, SD of GHbA1C &MPG for non- Diabetic controls

Parameters	GHbA1C		GHbA1C	
	Non-Diabetic	Diabetic	Non-Diabetic	Diabetic
Mean	4.76	8.44	89.40	223.02
SD	±0.62	± 2.07	±24.90	±73.80

The mean, SD of GHbA1C &MPG for non-Diabetic controls were 4.76 ± 0.62 and 89.40 ± 24.90 respectively.

The mean, SD of GHbA1C & MPG for Diabetic patients were 8.44 ± 2.07 and 223.02 ± 73.80 respectively showing the significant increase in Diabetic patients than that non-Diabetic controls.

The P value showed in the present study highly significant of less than 0.0001 in Non-Diabetic and Diabetic patients.

Table 2: Ratio of Non-Diabetic % controls and Diabetic Patients

Parameters	Ratio of Non-Diabetic % Controls	Ratio of Diabetic Patients %
Mean	18.78	26.42
	[42%]	[58%]

Pvalue of the Ratios is 0.0014 which is highly significant. The Mean,SD of Ratios are 18.78 in Non-Diabetic Controls and 26.42 in Diabetic Patients which showed the increase than controls.

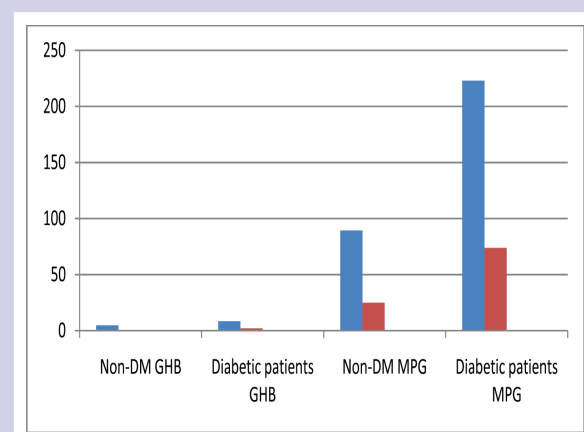
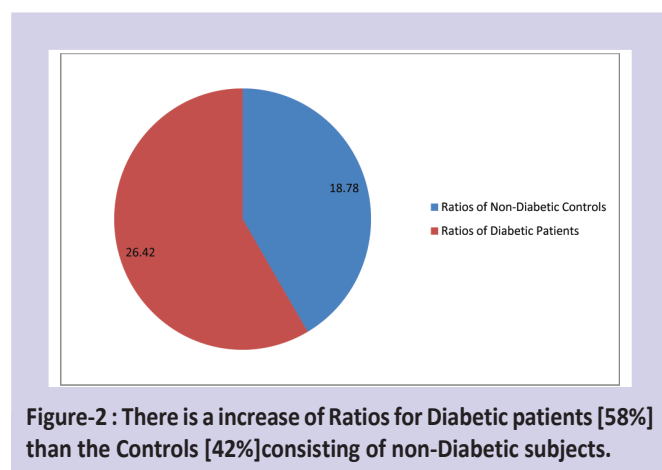


Figure-1: Shows the Mean SD of controls & Diabetic Patients for GHB & MPG

DISCUSSION

The global prevalence of diabetes mellitus is increasing rapidly. As the monitoring of glycemic status has been shown as the cornerstone of prevailing diabetes events and the measurement of glycated hemoglobin, is shown



to be predominantly as HbA1c, it is a common and useful test in the management of patients with diabetes.

The HbA1c is used to monitor long-term glycemic control, adjust therapy, assess the quality of diabetes care and predict the risk for the development of complications. Hence, HbA1c is the standard method for long-term glycemic control in diabetic patients, there are different methods for measurement of HbA1c and all laboratories do not use the reference method of which is high-performance liquid chromatography [HPLC] not due to unawareness but for the test is costlier and use of sophisticated instrument.

As Glycated haemoglobin (HbA1c) was initially identified as an "unusual" haemoglobin in patients with diabetes over 40 years ago.^[5] Many previous studies were in force, correlating blood glucose to HbA1C as an objective method for the measure of glycemic index in Diabetes.

There are various methods to measure Glyco hemoglobin.^[6,7] But the difference in reported values by these methods is high, making the comparison of these values very difficult.^[8,9]

Besides the ELISA Kit assays which is a dynamic research tool, there are many other methods for determination of GHB. It has been shown previously that estimation of Glycosylated HbA1C values has a direct relationship between mean blood glucose (MBG) and the development and progression of chronic diabetic complications.

The reference ranges for hemoglobin A1c levels in healthy adults is 4.8-5.7%. The diagnostic criterion for diabetes is a hemoglobin A1c level greater than or equal to 6.5%. In addition, various methods are under the influence of different factors such as types of anemia, pregnancy, splenectomy, transfusion and intake of medications (salicylates).^[10, 11, 12]

In reality HPLC method is easy to interpret and is an

economical method as it is also defined as a precise, cost-effective, functional and convenient method.^[13] The standard method of High-performance liquid chromatography (HPLC) is considered as reference method in accuracy and stability.

While HbA1c is the standard method for long-term glycemic control in diabetic patients, On the other hand, the HPLC device is very expensive, difficult and time consuming to work with; therefore, it needs professional personnel to work with, consequently making it impossible and not cost-effective for all laboratories. The calibration based on HPLC has been proven to enhance comparability among the various methods.^[14, 15]

Recommendations

1. HbA1c can be used as a diagnostic test for diabetes providing that stringent quality assurance tests are in place and assays are standardised to criteria aligned to the international reference values, and there are no conditions present which preclude its accurate measurement.
2. An HbA1c of 6.5% is recommended as the cut point for diagnosing diabetes. A value of less than 6.5% does not exclude diabetes diagnosed using glucose tests.
3. Quality of evidence assessed by GRADE: moderate
4. Strength of recommendation based on GRADE criteria: conditional^[16] but then, the HPLC device is very expensive, difficult and time consuming to work with; therefore, it needs professional personnel to work with, consequently making it impossible and not cost-effective for all laboratories. On the other hand, diabetic patients need HbA1C frequent check, and most of them cannot afford the cost of HbA1C by the HPLC method.

Numerous studies have compared different methods; therefore, with regard to the above reasons, it has been projected to compare three routine methods: 1. Boronate affinity binding (Nycocard) 2. Enzymatic(Diastyme), column chromatography (Biosystem), with HPLC method reports are consistent and correlated with those of HPLC so as to replace that in clinical laboratories.

When the means of the differential values between each method and HPLC in the ANOVA test were shown as follows: M=1.8, SD =1.09 for Nycocard-HPLC; M= 1.5, SD=1.08 for Biosystem-HPLC; M=1.3, SD=1.2 for Diastyme-HPLC. Pearson's correlation coefficient between HPLC and Nycocard; 0.76, HPLC and Diastyme; 0.75 and between HPLC and Biosystem was 0.68.

The review of the UKPDS, Action to Control Cardiovascular Risk in Diabetes, Advance and Veterans

Affairs Diabetes Trials estimated that the risks of the main complications of diabetes (diabetic retinopathy, diabetic nephropathy, diabetic neuropathy, and macrovascular disease) decreased by approximately 3% for every 1 mmol/mol decrease in HbA1c.^[17]

The Diabetic patients need HbA1C frequent check, and most of them cannot afford the cost of HbA1C by the HPLC method. It has been proven beyond doubt the estimation of Glycosylated HbA1C has a direct relationship between mean blood glucose (MBG) and the development and progression of chronic diabetic complications as shown in previous studies, as the GA/A1c ratio has been a unpredictable in clinical practice.

Though the ratio related to post lunch it is not confirmative. It has been noted in previous studies that the GHB is directly proportional to the ambient glucose concentration in circulating erythrocyte. As previously stated by theoretical models and clinical studies that, in a patient of stable control, half of its HbA1c levels will be formed in the current month before the test, 25% in the month before that, and the remaining 25% in the months 2 to 4.

The ratios of Glycosylated HbA1C measured by standard method to calculated MPG levels in the present study is useful as it ranges from 18.78 [42%] in controls consisting of non-Diabetics to 26.42 [58%] in the Diabetic patients and as according to previous studies shows the increase of more than 25% in the present study, though the cut point of 6.5% in diagnosis of Diabetes, less than that does not excluded the disease, hence the ratios over and above 18.78 are considered as significant in the present study. The ratios of these parameters can show the insight of advancing complications in Diabetic patients.

Therefore, in the present study, it has been shown that the ratios of Glycosylated Haemoglobin A1C to Mean plasma Glucose will prove to be the better parameter to assess the complications of Diabetes and contain the sequence of events occurring, which is calculative method, cost effective and easy to correlate the disease in Diabetes Mellitus type - 2 DM.

CONCLUSION

The GA/GHbA1C ratio is unpredictable but the ratio of GHbA1C/ Mean plasma glucose showed that it is better parameter to use in clinical practice for the containment of complications in Diabetic patients due to easy to interpret and as there is correlation between GHB and Mean plasma Glucose.

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CONFLICT OF INTEREST :

The authors declared no conflict of interest.

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