

Original Research Article

# Glycated Hemoglobin (HbA1c) - A Predictor of Glycemic Control and Diabetes Mellitus

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## ABSTRACT

Diabetes mellitus is a global problem and is on the increase in all walks of life .The increase prevalence of Diabetes mellitus type 2 is going to be the most in Asia in the next decade. The HbA1c level is currently one of the best ways to diagnose Diabetes mellitus. Level of HbA1c is in use to check glycemic control in diabetic and pre diabetic patients. Physicians provide treatment regime to reduce the risk associated with the development and progression of chronic complications of diabetes. HbA1c is taken to represent the glycemic control from few weeks to months. The majority of the diabetic patients in the present study show poor or uncontrolled with respect to HbA1c (>7%). The measurement of HbA1c is by HPLC method .Hence the interference by abnormal hemoglobin will be eliminated. However hemoglobin turnover rate should be taken into consideration. The risk for developing complications of Diabetes mellitus is high in the study group which warrants immediate preventive measures to reduce HbA1c level and thereby the onset of Diabetes mellitus.

**Key Words:** Diabetes mellitus, HbA1c (Glycated Hemoglobin), Glycemic control.

## INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterised by hyperglycaemia which threatens human wellbeing in every corner of the world. As per WHO calculation about 4% or 150 million of the world's adult population contracted Diabetes mellitus and might increase to 300 million by 2030. World Health Organisation also predicted that the prevalence of Diabetes mellitus would likely to increase the most in Asia in the coming century. The world wide prevalence of Diabetes mellitus was 2.8% in 2000 and is estimated to grow to 4.4% by 2030. This translates to a projected rise of Diabetes mellitus from 171 million in 2000 well over 300 million in 2030.

Diabetes has become a wide spread epidemic primarily because of the changing or altered life style of people and lack of exercise and awareness, stress and diet. Exercises have been considered as a cornerstone of diabetes management. Guidelines recommended that Diabetes mellitus patients perform at least 150min resistance exercise minimum 3 times per week. Exercise can increase insulin sensitivity, increase cardiovascular fitness and help to sustain weight loss. <sup>[1]</sup>

Diabetes mellitus is one of the many diseases that contribute to fallacies. Untreated and poorly controlled Diabetes mellitus can lead to micro and macro vascular complications, chronic diseases such as hypertension, kidney failure, loss of

eye sight, stroke, nephropathy and neuropathy and microalbuminuria. [2]

Glycated hemoglobin has been the key measure of glycemic control in diabetic patients for last two decades. It is considered to be the gold standard test and most widely accepted test for glycemic control among clinicians and patients. In 2009 the International Expert Committee recommended the use of HbA1c to diagnoses Diabetes mellitus with a threshold >6.5%. [3] The American Diabetic Association adopted HbA1c as <7% as an index of glycemic control in all Diabetes mellitus patients. [4] HbA1c reduction resulted in 42% reduction in the rise of CVD and 57% reduction in non-fatal heart attack, stroke or defects from cardiovascular cases. [5]

**METHODOLOGY**

A cross section study was carried out among type II Diabetes mellitus patients attending OP /IP of the hospital. The study period was January 2017 to December 2018. A total of 13467 samples were analysed for HbA1c using HPLC in Bio-Rad D10 hemoglobin testing system .All the patients

have been diagnosed and treated for Diabetes mellitus and its complications by the expert diabetes team of the reputed hospital .Blood was collected using EDTA vacutainer tubes. The values of HbA1c are expressed as HbA1c %.

Figure I a represent the percentage of Diabetes mellitus patients having good glycemic control i.e. <6.5% and those with uncontrolled or poorly controlled HbA1c >7%. Surprisingly those with good glycemic control is only 46% while uncontrolled or poorly controlled Diabetes mellitus patients contributes to 54% of the total patients of 2017 and 2018 included in the study.

Those patients with tight control were divided into 3 groups, 4% - 4.9%, 5% - 5.9%, and 6% - 6.9% of HbA1c .The percentage of Diabetes mellitus patients were 2.1 %,18%, and 26% respectively in the 3 groups. The results illustrated as diagram and also a table 1 Diabetes mellitus patients with poor glycemic control belong to various graph viz 7-7.9, 8-8.9, 9-9.9, 10-10.9, 11-11.9, >12 were 18, 12,8, 5.72,4.1,5.8 respectively (Table 1, Figure-2).

**Table 1: DISTRIBUTION OF TYPE IIDIABETES MELLITUS CASES BASED ON LEVELS OF HbA1c.**

| HbA1c %        | 4-4.9% |     | 5-5.9% |     | 6-6.9% |     | 7-7.9% |     | 8-8.9% |     | 9-9.9% |     | 10-10.9% |     | 11-11.9% |     | >12% |     |
|----------------|--------|-----|--------|-----|--------|-----|--------|-----|--------|-----|--------|-----|----------|-----|----------|-----|------|-----|
|                | 201    | 201 | 201    | 201 | 201    | 201 | 201    | 201 | 201    | 201 | 201    | 201 | 201      | 201 | 201      | 201 | 201  | 201 |
|                | 8      | 7   | 8      | 7   | 8      | 7   | 8      | 7   | 8      | 7   | 8      | 7   | 8        | 7   | 8        | 7   | 8    | 7   |
| January        | 11     | 8   | 103    | 105 | 147    | 185 | 96     | 125 | 71     | 88  | 50     | 55  | 33       | 30  | 18       | 25  | 29   | 35  |
| February       | 9      | 20  | 79     | 85  | 164    | 102 | 90     | 82  | 51     | 59  | 29     | 35  | 27       | 43  | 13       | 22  | 29   | 30  |
| March          | 6      | 17  | 75     | 66  | 136    | 131 | 125    | 103 | 49     | 63  | 47     | 44  | 32       | 29  | 19       | 36  | 24   | 39  |
| April          | 1      | 10  | 69     | 76  | 172    | 121 | 102    | 93  | 50     | 66  | 42     | 57  | 32       | 34  | 17       | 13  | 26   | 51  |
| May            | 14     | 13  | 112    | 104 | 163    | 131 | 88     | 89  | 59     | 62  | 45     | 38  | 27       | 29  | 32       | 25  | 41   | 44  |
| June           | 13     | 20  | 121    | 98  | 129    | 118 | 106    | 74  | 67     | 50  | 40     | 36  | 28       | 27  | 22       | 20  | 37   | 28  |
| July           | 8      | 7   | 129    | 80  | 167    | 126 | 107    | 96  | 83     | 76  | 49     | 39  | 38       | 26  | 24       | 18  | 29   | 35  |
| August         | 19     | 12  | 141    | 106 | 151    | 129 | 119    | 82  | 85     | 53  | 40     | 34  | 37       | 34  | 21       | 26  | 34   | 25  |
| September      | 25     | 13  | 127    | 92  | 177    | 110 | 132    | 85  | 84     | 54  | 64     | 43  | 33       | 20  | 24       | 11  | 33   | 26  |
| October        | 11     | 9   | 127    | 86  | 221    | 130 | 138    | 83  | 85     | 53  | 56     | 36  | 33       | 34  | 22       | 20  | 44   | 29  |
| November       | 10     | 6   | 148    | 77  | 178    | 134 | 133    | 103 | 86     | 62  | 59     | 46  | 37       | 29  | 38       | 24  | 24   | 30  |
| December       | 9      | 9   | 122    | 97  | 182    | 139 | 144    | 73  | 89     | 52  | 59     | 30  | 41       | 30  | 24       | 25  | 34   | 23  |
| Sum            | 136    | 144 | 135    | 107 | 198    | 155 | 138    | 108 | 859    | 738 | 580    | 493 | 398      | 365 | 274      | 265 | 384  | 395 |
| Total Sum      | 280    |     | 2425   |     | 3543   |     | 2468   |     | 1597   |     | 1073   |     | 763      |     | 539      |     | 779  |     |
| Percentage (%) | 2.1    |     | 18     |     | 26.3   |     | 18.3   |     | 11.8   |     | 7.9    |     | 5.6      |     | 4.1      |     | 5.7  |     |

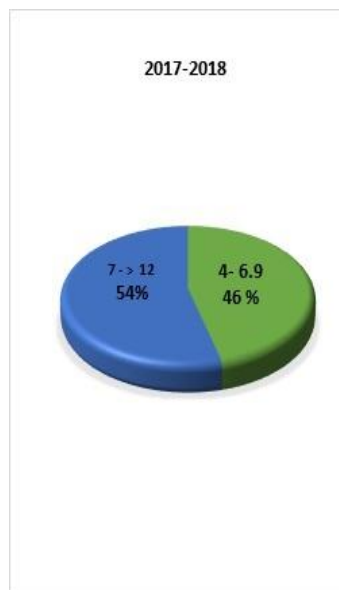


Figure No. 1:- Distribution of Type2 Diabetes mellitus based on glycemic control.

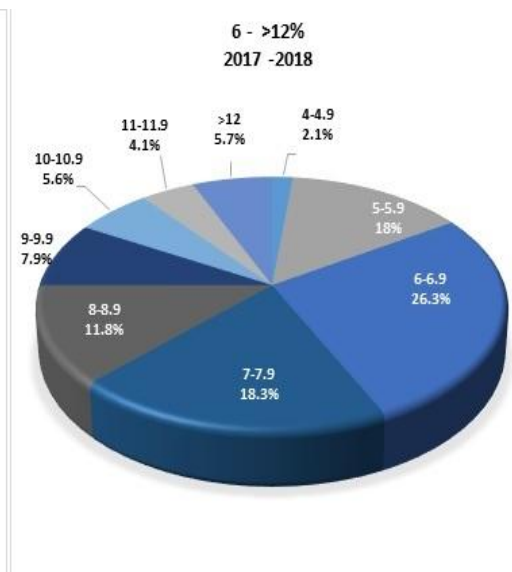


Figure No. 2 Distribution of Type 2 diabetes mellitus into various groups based on levels of HbA1c.

## DISCUSSION

Diabetes mellitus is a public health problem and has become a concern to all levels of society. The development of chronic vascular complications of diabetes such as retinopathy, neuropathy and cardiovascular diseases is intimately linked to the level of glycemic control attained by the individuals with diabetes. Therefore it is essential to have an index of the long term glycemic control in diabetic patients, which in turn can be used to guide therapy and predict likelihood of the complications.

Glycated hemoglobin has been the key measure of glycemic control in diabetes patients for last two decades. It is considered to be the gold standard and most widely accepted test of glycemia control among clinicians and patients. The glycated hemoglobin concentration levels are also more closely related to the risk of chronic complications than single episodic glucose level. In 2009 the International Expert Committee recommended the use of HbA1c to diagnose Diabetes mellitus with a threshold of >6.5%. [6]

The ADA recommended goal for HbA1c is <7% in all diabetic patients. The same level is recommended for prevention of cardiovascular disease in people with Diabetes mellitus. The ideal HbA1c goal for

individual diabetic patients is as low as <6% without causing significant hypoglycaemia. [7]

Glycated hemoglobin is formed by non-enzymatic glycation of N terminal valine of  $\beta$  chain of hemoglobin. Different lab techniques and many clinical conditions may result in under estimation and over estimation of HbA1c.

Clinicians should interpret very low (<4%) or very high (>15%) results with caution and concurrent diseases should be given due importance. Patients with HbA1c between 6 and 6.5% are at very high risk of developing Diabetes mellitus and the risk increases substantially as the value increases. [8]

The normal level of HbA1c is 3% to 5.5% and high normal 5.6 to 6% in non-diabetic and diabetics >6.5% American Diabetic Association adopted <7% HbA1c for glycemic control and in this study more than half the patients (53.9%) have >7% HbA1c. This is alarming as they are at high risk for developing multiple complications as well as cardiac diseases. In the patients with glycemic control (46.1%) has HbA1c 4 - 6.9% indicating the chances of developing complications is high.

Larger volume of data from diverse populations has now established A1c level

associated with an increase in the prevalence of moderate neuropathy and provides strong justification for assigning a cut off A1c level at point of  $\geq 6.5\%$  for the diagnosis of Diabetes mellitus. The A1c level of 6.5% is sufficiently sensitive and specific to identify individuals who are at high risk for developing retinopathy and should be diagnosed as diabetic as per the National glycohemoglobin study programme. [9]

HbA1c provides a better biological index than fasting blood glucose as would be expected with a measure of chronic glycaemia levels compared with glucose concentration that are known to fluctuate within and between days. In short it provides a better index of overall glycemic exposure and risk for long term complication with no need for fasting or timed samples and relatively unaffected by acute perturbations in glucose levels.

In the present study majority of the patients fall in the high risk levels for developing short and long term complications of Diabetes mellitus. These patients need constant attention and treatment for proper health care.

Although HbA1c is a more feasible biological index for assessing glycemic control any condition that changes RBC turnover such as haemolytic anaemia, chronic malaria, sickle cell anaemia, blood transfusions G6PD deficiency sickle cell anaemia, thalassemia will lead to spurious A1c results. These conditions are highly prevalent in certain parts of India. Besides handling persistence of foetal Hb, folate, B12 or Iron deficiency, splenectomy also show elevated HbA1c. [10] Alcoholism, lead poisoning, opiate addiction excessive use of salicylates and pregnancy can lead to falsely elevated HbA1c levels. Age and regional variations too influence HbA1c levels but no studies have been carried out yet. There is not sufficient data on whether Indians are high or low glycaters. [11] In the present study majority of the patients possess HbA1c level beyond the cut of point of

6.5%. Hence the possibility of developing complications are quite high.

Diabetes mellitus is a public health problem and the health care authorities and the Government should be aware of the situation. Majority of Diabetes mellitus patients can develop micro and macro vascular complications, loss of eye sight, micro albuminuria and in case of infections even amputations. For assessing glycemic control HbA1c must be measured once in three months and it is a costly test.

The data of the present study clearly point out that the Diabetes mellitus patients in general are at high risk level and providing adequate health care to them is a costly affair for the health care professional and administrators. The WHO has made it very clear that the prevalence of Diabetes mellitus is going to be increased worldwide and the proportion is going to be high in Asia. This is alarming specially in a country like India having limited resources poor awareness of the significance and importance of HbA1c. To overcome this or at least reduce the intensity, public should be made aware of the specific and significant role of HbA1c in controlling or preventing short and long term complication of Diabetes mellitus. The present situation of high risk prevalence of Diabetes mellitus complications if unfolded can put enormous burden on already stretched health care resources which could easily be avoided by intensive control of Diabetes mellitus via glycemic control.

The Delhi Diabetes community and Diabetic care Asian Survey reported that 54% of the Diabetic population have HbA1c  $> 8\%$  and are prone to severe last stage complications. [12] This is in agreement with the present study.

The clinicians, health care professionals, dieticians, firm and voluntary organisations should join hand in hand and come out to act with a single goal of creating public awareness regarding glycemic control to lower HbA1c to 4.5 -6% with preventive life style choices, integrated medication therapy which alone could pave

the way to lead a normal life free of Diabetes mellitus.

## CONCLUSIONS

HbA1c has been universally accepted as an index of glycemic control and major therapeutic decisions are taken based on it. There is increasing interest in using HbA1c for the diagnosis of diabetes as well. However measurement of HbA1c level as sole tool for assessing the diabetic status could not be used clinically since level of glycated hemoglobin depends on various factors specifically RBC turnover, hemoglobinopathies, Sickle cell anaemia, thalassemia etc. and several drugs. Haematological status should always be taken into account while interpreting HbA1c levels. Measurement of HbA1c should be by HPLC technique.

The present study revealed that 56% of type 2 Diabetes mellitus patients attending our tertiary level hospital has poor diabetic control with HbA1c level of >7%. This clearly points out that the Diabetes mellitus patients are at high risk for developing micro and macro vascular complications myocardial infarction, renal failure and CVDS. It is important that preventive activities be started on a war footing by health education and counselling activities to reduce and overcome the disaster. Clinicians, health care professionals, volunteer organisations and dietician join hand in hand and work with a common goal so that not only diabetic population but also the public at large who have upper high level of HbA1c can attain HbA1c <6% and have life free of diabetes mellitus.

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