

EVALUATION OF AWARENESS ABOUT THE ROLE OF GLYCATED HEMOGLOBIN AS A MARKER IN DIABETIC PATIENTS

INDIRA R.SAMAL¹, BHAVANA R. THAKURDAS² & AMARJIT VIJ³

^{1,2}Associate Professor, Department of Biochemistry, Punjab Institute of Medical Sciences, Jalandhar, India

³Professor, Department of Medicine, Punjab Institute of Medical Sciences, Jalandhar, India

ABSTRACT

Background

The prevalence of type II diabetes is increasing at an alarming rate. Early detection, intervention and control of blood sugar can prevent systemic complications and morbidity. Glycated hemoglobin (HbA1c) is a test that does not require fasting and with fewer perturbations with stress, diet and exercise. It is now widely recognized for the diagnosis of diabetes mellitus (DM) and as an indicator for the efficacy of treatment. Limited data is available about the awareness of the role of glycated hemoglobin (HbA1c) in northern India

Material and Methods

Data was collected between 1/5/14 to 31/3/15 from 500 diabetic patients both male and female aged 20-80 years attending the outdoor patient department at Punjab Institute of Medical Sciences, Jalandhar, India by interview method. The questionnaire consisted of both open ended and close ended questions and the data was analyzed by SPSS ver11.0.

Results

Most (50%) patients knew blood sugar estimation to be the test for DM but did not know the desirable levels. However more than 75% of the patients did not know the use, frequency and normal ranges of HbA1c.

Conclusions

Apart from biochemical analysis of blood sugar and HbA1c, educating the general population about HbA1c, its use, range and frequency would help the clinicians in managing the patients in a holistic manner. Data presented in this study would be useful to the healthcare policy makers to educate and create awareness in the general population about the control of blood sugar in DM.

KEYWORDS: Awareness, Diabetes, Glycated Hemoglobin

INTRODUCTION

Background

Diabetes Mellitus (DM), often referred to as diabetes—is a condition in which the body either does not produce enough insulin, or does not properly respond to insulin(1). The prevalence of type 2 diabetes is increasing at an alarming rate. Current projections suggest that the absolute number of cases worldwide may double over the next two decades (2). With the rapid economic development, elevated standard of living, dietary shifts, lifestyle alterations, and ageing, diabetes mellitus (DM) has become an important public health problem worldwide(3-5), which is estimated to be the third most

challenging disease threatening public health after malignant tumors and cardio cerebral vascular diseases(6). Diabetes mellitus is now the leading cause of cardiovascular, renal and other serious comorbidities not only in old but also young adult (7-9). It has been estimated that the global number of individuals with diabetes will double from 171 million in 2000 to 366 million in 2030 among adults aged ≥ 20 years (10). Data from European countries have indicated that the health care expenditure for patients with diabetes mellitus was significantly higher than for those who were not diagnosed with this disease (11-13).

Early detection and intervention in diabetes is now considered one of the most important public health agendas(1). This leads on to hyperglycemia, which is the basic cause of systemic complications associated with the disease. Strict control of blood sugar remains the pivot in the decreased incidence of complications. Good glyceic control is essential in preventing diabetic complications (1, 14).

Fasting plasma glucose (FPG) is a simple, easy, inexpensive, and widely available to general population and has been most frequently used to identify subjects at high risk of diabetes. (15). The 2-h plasma glucose after oral glucose tolerance test (OGTT) is also useful to identify subjects of impaired glucose tolerance. However, the OGTT is not common in clinical practice, because not only is it difficult to perform but also the cost and demands on participants' time is excessive (16).

The level of glycated hemoglobin (HbA_{1c}) provides a measure of the glyceic control of diabetes patients during the previous 2–3 months (17). (HbA_{1c}), an indirect measure of mean blood glucose, does not require fasting, and is more reproducible than FPG (15).

Glycated hemoglobin should be measured in all individuals with DM during their initial evaluation and as part of their comprehensive diabetes care (18). It is the primary predictor of long-term complications of DM (19). Measuring glycated hemoglobin, the "gold standard" method for assessing glyceic control, is therefore fixed firmly in the sights of the clinical target setters (20)

In the normal 120 day life span of the red blood cells (RBCs,) glucose molecules react with Hemoglobin, forming glycated hemoglobin. Measuring HbA_{1c} can reveal as to how high the blood glucose has been on an average, over the past 8-12 weeks. A normal non-diabetic HbA_{1c} value is 3.5-5.5%. In diabetics, range of 6.5% to 7% is good. In individuals with poorly controlled diabetes, the quantity of this glycated Hb is much higher than in healthy people. A buildup of glycated Hb within the red blood cells, therefore, reflects the average level of glucose to which the cells have been exposed during their life cycle. The glyceic goal is to achieve HbA_{1c} as close to normal as possible, without developing significant hypoglycemia. In general, the target HbA_{1c} should be $<7.0\%$ with a more stringent target ($<6\%$) for many patients. A higher HbA_{1c} goal may be appropriate for the very young or old or in individuals with limited life spans or comorbid conditions (21). Besides the average level of HbA_{1c}, certain changes in HbA_{1c} levels and HbA_{1c} at different points in time can possibly have different implications for the clinician and in studies of the relation between HbA_{1c} and diabetic complications (22). The major consideration is the frequency and severity of hypoglycemia, since this becomes more common with a more stringent HbA_{1c} goal. The advantages of doing HbA_{1c} assessment are non-requirement of fasting, with fewer perturbations with stress, diet and exercise. It captures the chronic hyperglycemia better than fasting glucose levels. The analytical variability is similar with estimation of blood glucose levels (23). Due to the recent advancement of HbA_{1c} measurement, the American Diabetes Association (ADA) report in 2009(24) advocated that, the diagnosis of diabetes may be conveniently based on HbA_{1c} $\geq 6.5\%$. Diabetes is defined according to the 2010 American Diabetes

Association (ADA) criteria : FPG \geq 7.0 mmol/l, HbA_{1c} values \geq 6.5%, or both, or treatment by oral antidiabetic drugs or insulin.(25) Doctors' awareness of this measure has been shown to be associated with better glycemic control for their patients,(26) and patients are invited to evaluate their own achievements in controlling their diabetes in terms of this measure.(27).With this background, we made a random assessment of HbA_{1c} in a sample population, using clinical questionnaire on awareness about glycated hemoglobin and diabetes.

MATERIAL AND METHODS

After obtaining institution Ethical Committee approval, we interviewed the diabetic patients who came to the outpatient department at Punjab Institute of Medical Sciences, Jalandhar, India from 1/5/14 to 31/3/15. Most of the patients were known cases of diabetes that had come for follow-up and for biochemical investigations. A preinformed consent was taken from all the participants and the patients were interviewed using a simple criterion. Patient identifiers like name, age date of birth and medical record number were used to generate the data for analysis.

All patients with diagnosis of DM aged between 20-80 years, graduates and who had come for checkup for diabetes during above period were included in the study. Patients with history of chronic persistent illness, malignancy, thalassemia, anemia and pregnancy were excluded from the study. A pretested questionnaire consisting of both open ended and closed ended questions was used for the study. Data was collected by interview and questionnaire being filled by the participants and the investigators. Collected data was tabulated in Microsoft excel sheet and was analyzed in SPSS ver11.0. Additional data like patient demography, appropriate past medical history, dietary habits', lifestyle and duration and treatment of diabetes was also collected.

RESULTS

Five hundred patients were found to be eligible for the study. Of these, data of 12 patients was excluded as they could not decipher the questionnaire; hence 488 patients were included in the analysis.

Patient characteristics has been described in Table 1

Table 1: Baseline Patient Characteristics Included in Analysis

	Female	Male	Total
N	198	290	488
Average age (Years)	34 \pm 13.1	52.3 \pm 14.3	43.1 \pm 13.7

Mean age of the subjects was 43 years.(83%) knew blood sugar estimation (FBS, PPBS, and RBS) was done for evaluating control of diabetes but 60 % had no knowledge of the levels of blood sugar that have to be maintained (figure 1 and 2)

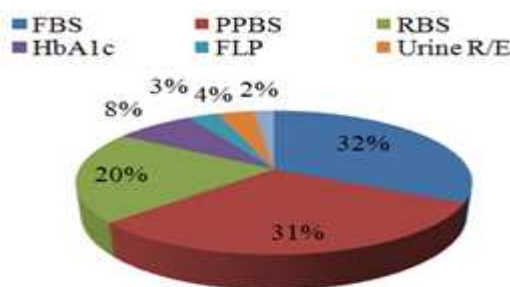


Figure 1: Do you know of any Tests for Diabetes?

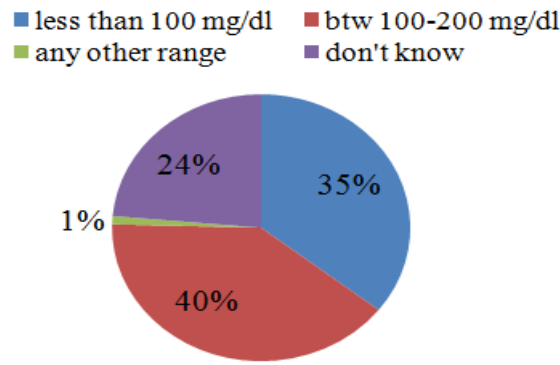


Figure 2: Are you Aware How Much should be Your Blood Sugar?

77% of patients were not aware of the availability or the significance of HbA1c as a marker of DM. Among these 92% were ignorant about the normal levels of HbA1c and 79% did not have any knowledge about the frequency of HbA1c testing. (Figure 3, 4, 5)

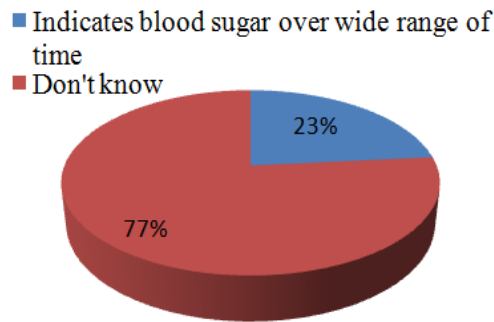


Figure 3: What is Glycated Hemoglobin or HbA1c

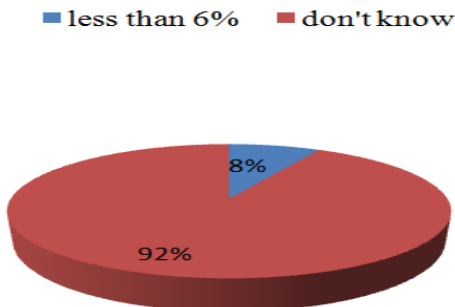


Figure 4: Are You Aware about the Normal Range for HbA1c?



Figure 5: Frequency of HbA1c Test

DISCUSSIONS

Fewer than 20% of the subjects with known diabetes had had their HbA1c tested during the past year. The American Diabetes Association recommends that HbA1c be tested at least semiannually in individuals with diabetes who have stable glycemic control and quarterly in patients whose therapy has changed or who are not meeting glycemic goals (28). The frequency of measurement of HbA1c has been directly linked to level of glycemic control in various populations. In a case control study of 193 subjects with type 2 diabetes seen over a 6-month period in a rural practice in the United States, good control of diabetes based on HbA1c levels was positively associated with adherence to recommendations on the frequency of monitoring of HbA1c.(29) In a cross-sectional study of 1,511 patients recruited from 15 hospitals in China, poor glycemic control was found to be associated with a lower frequency of monitoring of HbA1c.(30) The extremely low frequency of HbA1c is worrying as it indicates that large proportions of the population with diabetes in India do not have recent data on their status of glycemic control, leading to delay in intensification of treatment and accumulation of avoidable glycemic burden.

Various studies from India (31) have confirmed the association of HbA1c with prevalent diabetic complications (32, 33, 34) as well as with cardiovascular disease.(31) In accordance with current guidelines in the management of diabetes in the ICI study also, most doctors agreed that HbA1c testing is crucial.

However, the advice for HbA1c testing was given in only in 79% as against that of FPG & PPG in 97% & 96% of patients respectively. Although HbA1c was considered as an important parameter in diabetes management but the emphasis on this test while making the patient understand the importance of various tests was relatively very low. When it came to patient's perception, in 19% of cases HbA1c was felt to be a routinely advised test. Moreover only 1/3rd of the patients were aware of the HbA1c test. Many doctors felt that standardization of HbA1c in laboratories is not reliable and therefore preferred only FPG and PPG measurements. Even when HbA1c tests were requested, they were done only once or twice a year (31)

Result oriented organized programmes involving patient education, updating medical fraternity on various developments in the management of diabetes and providing them the opportunity to use and analyze these newer treatment options in the form of observational studies is required so that we can combat the diabetes epidemic which is currently threatening to affect the lives of millions of people in India (35)

The use of fasting plasma glucose for diabetes diagnosis is limited given the high prevalence of stress hyperglycemia and frequent use of glucocorticoid medications in inpatients(36) oral glucose tolerance test for inpatient diabetes screening is resource intensive and impractical(37) HbA1c testing is superior for the inpatient diagnosis of diabetes(38) however, sensitivity may be lowered by significant renal impairment, anemia, blood transfusions, and hemoglobinopathies, while prolonged stress hyperglycemia may produce false-positive results.(39, 40)These conditions are unlikely to be in numbers large enough to affect overall screening.(41) HbA1c has the advantage of aiding both diabetes diagnosis and management.

In 2009, the International Expert Committee (42) which comprised members appointed by the ADA, the European Association for the Study of Diabetes, and the IDF, recommended that diabetes be diagnosed by measurement of hemoglobin A_{1c} (HbA_{1c}), which reflects long-term blood glucose concentrations . The ADA (43) and the WHO have endorsed the use of HbA_{1c} for diagnosis of diabetes.

LIMITATIONS

We relied on interviews/questionnaire methods. Additionally we further want to assess the knowledge about diet and lifestyle modifications among the DM patients and the general population as a whole.

CONCLUSIONS

A clinician must customize treatment modalities for a patient according to the knowledge and awareness of the disease. The knowledge and awareness of HbA1c would also help a clinician in managing a patient in a holistic manner. Data presented in this study may help the clinician and health care policy makers to create awareness and knowledge about DM in this part of India. Study also shows that there is no significant difference in awareness of HbA1c according to the educational status. The knowledge and awareness needs to be reinforced through health awareness programmes at all the levels. These need to be carried out at the PHC's sub-centers and through health workers. Patient from different town and cities from same state should be studied to come to more authentic conclusion. Due to feasibility and time constrains we could not do this as a part of our exercise. Such multicentric studies can be done which can help the clinicians to create awareness and educate the community.

REFERENCES

1. UK Prospective Diabetes Study (UKPDS) Group. "Intensive blood-glucose control with sulphonylureas compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33)." *Lancet*. 1998; 352:837–53.
2. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Res Clin Pract*. 2010; 87:4–14.
3. Zimmet P, Alberti KGMM. Global and societal implications of the diabetes epidemic. *Nature*. 2001; 414(6865):782–787.
4. Motala AA, Omar MAK, Pirie FJ. Epidemiology of type 1 and type 2 diabetes in africa. *Journal of Cardiovascular Risk*. 2003; 10(2):77–83.
5. Engelgau MM, Geiss LS, Saaddine JB, et al. The evolving diabetes burden in the United States. *Annals of Internal Medicine*. 2004; 140(11):945–950.
6. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. *Diabetes Care*. 1998; 21(9):1414–1431.
7. Dandona P, Aljada A, Chaudhuri A, Mohanty P, Garg R. Metabolic syndrome: a comprehensive perspective based on interactions between obesity, diabetes, and inflammation. *Circulation*. 2005; 111:1448–1454.
8. Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. *Diabetes Care*. 2005; 28:1769–1778.
9. Fox CS, et al. Trends in the incidence of type 2 diabetes mellitus from the 1970s to the 1990s: the Framingham Heart Study. *Circulation*. 2006; 113:2914–2918.

10. Wild S, Roglic G, Green a, Sicree R, King H. Global Prevalence of Diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*.2004; 27(5):1047–1053.
11. Jönsson B. Revealing the cost of type II diabetes in Europe. *Diabetologia*.2002; 45(7):5–12.
12. Ricordeau P, Weill A, Vallier N, et al. The prevalence and cost of diabetes in metropolitan France: what trends between 1998 and 2000? *Diabetes and Metabolism*. 2003; 29(5):497–504.
13. Ettaro L, Songer TJ, Zhang P, Engelgau MM. Cost-of-illness studies in diabetes mellitus. *Pharmaco Economics*. 2004; 22(3):149–164.
14. DCCT Study Group. The Effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993; Sep 30; 329(14):977–986.
15. International Expert Committee. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. *Diabetes Care*. 2009; 32:1327–1334.
16. The expert committee on the diagnosis and classification of diabetes mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2003; 26:S5–20.
17. Jeffcoate SL. Diabetes control and complications: the role of glycated haemoglobin, 25 years on. *Diabet Med*. 2004; Jul; 21(7):657–665.
18. International Expert Committee Report on the role of the A1C assay in the diagnosis of diabetes. *Diabetes Care*. 2009; 32:1327–34.
19. Greci Laura S, Kailasam Mala. “Utility of HbA1c Levels for Diabetes Case Finding in Hospitalized Patients with Hyperglycemia” *Diabetes Care*. 2003; 26(4):1064–68.
20. British Diabetic Association. Recommendations for the management of diabetes in primary care. London: BDA, 1993.
21. Rohlfing CL, Wiedmeyer HM, Little RR, England JD, Tennill A, Goldstein DE. “Defining the Relationship between Plasma Glucose and HbA1c, Analysis of glucose profiles and HbA1c in the Diabetes Control and Complications Trial,” *Diabetes Care*. 2002; 25:275–78.
22. Lind M, Odén A, Fahlén M, Eliasson B. A Systematic Review of HbA1c Variables Used in the Study of Diabetic Complications, *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. 2008:282–293.
23. Enzo bonora, Jaakotuomilehto. The Pros and Cons of Diagnosing Diabetes with A1C. *Diabetes Care*.May 2011; 34(Supplement 2):S184–S190.
24. Sato KK, Hayashi T, Harita N, Yoneda T, Nakamura Y, et al. Combined measurement of fasting plasma glucose and A1C is effective for the prediction of type 2 diabetes: the Kansai Healthcare Study.*Diabetes Care*. 2009; 32:644–646.
25. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes care*.2011; 34:S62–69.
26. Larsen ML, Horder M, Morgensen EF. Effect of long-term monitoring of glycosylated haemoglobin levels in insulin-dependent diabetes mellitus. *N EnglJMed* 1990; 323:1021-5.

27. American Diabetes Association. Standards of medical care for patients with diabetes mellitus. *Diabetes Care* 1994; 17:616-8.
28. 15. American Diabetes Association: Executive summary: standards of medical care in diabetes—2012. *Diabetes Care* 2012; 35(Suppl 1):S4–S10.
29. 21. Parcero AF., Yaeger T., Bienkowski RS.: Frequency of monitoring hemoglobin A1C and achieving diabetes control. *J Prim Care Community Health* 2011;2:205–208
30. 22. Fu C., Ji L., Wang W., Luan R., and Chen W., Zhan S., Xu B.: Frequency of glycosylated hemoglobin monitoring was inversely associated with glycemic control of patients with Type 2 diabetes mellitus. *J Endocrinol Invest* 2012; 35:269–273.
31. 44. Rema M, Premkumar S, Anitha B, Deepa R, Pradeepa R, Mohan V. Prevalence of Diabetic Retinopathy in Urban India: The Chennai Urban Rural Epidemiology Study (CURES) Eye Study-1. *Invest Ophthalmol Vis Sci* 2005; 46:2328-33.
32. 51. Ranjit Unnikrishnan I, Rema M, Pradeepa R, Deepa M, Shanthirani CS, Deepa R, Mohan V. Prevalence and risk factors of diabetic nephropathy in an Urban South Indian population
33. 57. Pradeepa R, Rema M, Vignesh J, Deepa M, Deepa R, Mohan V. Prevalence and risk factors for diabetic neuropathy in an urban south Indian population: the Chennai Urban Rural Epidemiology Study (CURES-55). *Diabet Med* 2008; 25:407-12.
34. 65. Dilley J, Ganesan A, Deepa R, Deepa M, Sharada G, Williams OD, Mohan V. Association of A1C with cardiovascular disease and metabolic syndrome in Asian Indians with normal glucose tolerance. *Diabetes Care* 2007; 30:1527-32.
35. Shashank R Joshi, AK Das, VJ Vijay, V Mohan. Challenges in Diabetes Care in India: Sheer Numbers, Lack of Awareness and Inadequate Control. *JAPI*; 56 • JUNE 2008:444-450.
36. 18. Wexler DJ, Meigs JB, Cagliero E et al. Prevalence of hyper- and hypoglycemia among inpatients with diabetes: a national survey of 44 U.S. hospitals. *Diabetes Care* 2007; 30:367–9. Doi: 10.2337/dc06-1715.
37. 19. d'Emden MC, Shaw JE, Colman PG et al. The role of HbA1c in the diagnosis of diabetes mellitus in Australia. *Med J Aust* 2012; 197:220–1. doi:10.5694/mja12.10988.
38. Valentine NA, Alhawassi TM, and Roberts GW et al. Detecting undiagnosed diabetes using glycosylated haemoglobin: an automated screening test in hospitalised patients. *Med J Aust* 2011; 194:160–4.
39. 20. Wexler DJ, Nathan DM, Grant RW et al. Prevalence of elevated hemoglobin A1C among patients admitted to the hospital without a diagnosis of diabetes. *J Clin Endocrinol Metab* 2008; 93:4238–44. doi:10.1210/jc.2008-1090.
40. 21. Gallagher EJ, Le Roith D, Bloomgarden Z Review of hemoglobin A (1c) in the management of diabetes. *J Diabetes* 2009; 1:9–17. doi:10.1111/j.1753-0407.2009.00009.

41. 22. Bennett CM, Guo M, Dharmage SC HbA (1c) as a screening tool for detection of type 2 diabetes: a systematic review. *Diabet Med* 2007; 24:333–43. doi:10.1111/j.1464-5491.2007.02106.
42. 20. The International Expert Committee International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. *Diabetes Care* 2009; 32:1327–34.
43. 21. ADA Standards of medical care in diabetes—2010. *Diabetes Care* 2010; 33(Suppl. 1):S11–61.

