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Original article

Frequency of Glycemic Control In Type 2 Diabetes Mellitus Patients Assessed By Glycated Hemoglobin and Estimated Average Blood Glucose

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ABSTRACT:

Objective: To estimate HbA1c (%) in type 2 Diabetes mellitus (DM) patients to calculate estimated average blood glucose (eAG) and to correlate them with fasting and post prandial blood glucose level.

Materials and methods: HbA1c was estimated in hemolysate by nephelometric method followed by National Glycohemoglobin Standardization Program (NGSP) protocol with MISPA-I2 smart card system in 104 type 2 DM patients. FBG and PPBG were simultaneously determined in serum of patients. The calculation was done by using formula eAG (mg/dl): (28.7*HbA1c)-46.7 given by NSGP/DCCT guideline. The categorization of glycemic control was made as HbA1c ≤5.9% (very good glycemic control), HbA1c between 6.0 and 6.9 % (good glycemic control), HbA1c between 7.0 and 7.9 % (poor glycemic control), HbA1c ≥ 8% (bad glycemic control).

Results: The age-wise categorization of type 2 DM shows maximum frequency of patients of 21 (20.19 %) comprising 10 (9.61 %) male and 11(10.57 %) female respectively in age group 41-60 whose HbA1c and eAG were (7.6 ± 2.9 %) and eAG (172.66 ± 81.79 mg/dl) respectively. The statistically significant correlation was observed between HbA1c/eAG with FBG and PPBG ($p<0.001$).

Conclusion: The high frequency of patients in categories >8.0 % HbA1c and increased eAG signifies the bad glycemic control and project to the complication associated with DM later in life.

KEYWORDS: HbA1c; estimated average glucose; glycemic control; Type 2 DM.

Statement of Originality of work: The manuscript has been read and approved by all the authors, the requirements for authorship have been met, and that each author believes that the manuscript represents honest and original work.

INTRODUCTION

Glycated hemoglobin concentrations reflect time-averaged blood glucose during the previous 2-3 months and are used as the gold standard for long term follow up of glycemic control[1]. The glycated hemoglobin (HbA1c) is non-enzymatic condensation of glucose to the valine residue of β-hemoglobin to form aldimine and then by amadori rearrangement to ketoamine. Diabetes Control and Complication Trial (DCCT), a great extent study, has demonstrated that the 10%

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stable reduction in HbA1c determines a 35% risk reduction for retinopathy, a 25-44% risk reduction for nephropathy and a 30% risk reduction for neuropathy[1-3]. Patients should clearly understand the relationship between high HbA1c results and health risks, but this should be explained in the context of the importance of having good daily glycemic profiles, which can be so important to quality of life by reducing the variability of blood glucose during the day[4].

The nephelometry methology is reliable, time saving and non tedious method for estimation of HbA1c following National Glycohemoglobin Standardization Program (NGSP) guideline. It is based on the amount of agglutination that is proportional to the amount of HbA1c absorbed onto the surface of latex particles. In this method total hemoglobin determination is not required and direct result in % HbA1c can be obtained from the analyzer. It is completely automatic and presents an excellent reproducibility in different laboratories[5].

Understanding this relationship between HbA1c and estimated average glucose (eAG) can help patients with diabetes and their health-care providers set day-to-day targets for average glucose based on HbA1c goals. Our paper has projected the frequency of glycemic control categorized as very good glycemic control (≤5.9 %), good glycemic control (6.0-6.9 %), poor glycemic control (7.0-7.9 %) and bad glycemic control (≥8.0 %). The present study has shown the association of glycemic control as assessed by HbA1c and eAG in Type 2 Diabetes mellitus with FBG and PPBG.

MATERIALS AND METHODS

This is a cross-sectional study carried in Type 2 diabetes mellitus patients (n=104), visiting National Medical College Teaching hospital (NMCTH), Birgunj, Nepal, confirmed by Fasting Blood Glucose (FBG) based on World Health Organization (WHO) criteria during period of November 2013 to December 2014. Fasting and Post prandial blood Glucose concentration were determined for the patients on same day through venipuncture into sterile tubes and fasting blood was also dispensed in the tube containing the tripotassium salt $EDTAK_3$ and processed within 2 hours for the measurement of HbA1c by using nephelometry method[6]. This method utilizes the interaction of antigen and antibody to directly determine the HbA1c in whole blood. Total hemoglobin and HbA1c have the same non specific absorption rate to latex particle. When mouse antihuman HbA1c monoclonal antibodies is added (R2), latex HbA1c – mouse antihuman HbA1c antibody complex is formed. Agglutination occurs when goat antimouse IgG polyclonal antibody interacts with the monoclonal antibody. The amount of agglutination is proportional to the amount of HbA1c absorbed onto the surface of latex particles. The amount of agglutination is measured to calculate HbA1c % from a calibration curve.

The test procedure and the calibration data followed National Glycohemoglobin Standardization Program (NGSP) method with MISPA-I2 smart card system. The smart card was inserted to card reader slot & display will be prompted to add R1+Sample.180 µL R1 & 5 µL sample was pipeted to cuvet & than placed into cuvet holder. After incubation display will be prompted to add R2. 60 µL R2 was pipeted using attached sensor pipette to the cuvet. The result will show in the display and printed out.

The relationship between eAG and HbA1c based on linear regression analysis following: eAG (mg/dl)= (28.7*HbA1c)-46.7, r^2=0.84.[7]

Criteria for evaluation of the metabolic control for HbA1c were given as HbA1c ≤5.9% (very good glycemic control), HbA1c between 6.0 and 6.9 % (good glycemic Control), HbA1c between 7.0 and 7.9 % (poor glycemic Control), HbA1c ≥8% (bad glycemic control). Protective values of HbA1c to chronic complications are considered <7%.

STATISTICAL ANALYSIS

Data were processed with the statistical software; SPSS version 16. The mean and SD were presented as continuous variables and categories were expressed as percentages. For comparison of the mean values of categories, the student's t-test and Pearson's correlation were selected. The statistically significant level is set at p-value <0.05.

RESULTS

Table 1 shows the distribution of glycemic control in type 2 DM patients where the maximum cases fall in HbA1c% ≥8 % in age group 41-60 years with frequency of 21 (20.19 %) comprising 10 (9.61 %) male and 11 (10.57 %) female respectively followed by HbA1c ≤5.9%, 6-6.9% and 7-7.9% with frequency 15 (14.42%), 14 (13.46%) and 6 (5.76%) respectively. Similarly, maximum cases 9 (8.65 %) with HbA1c≤5.9% followed by ≥8.0 and 7-7.9% with frequency of 8 (7.69%) and 0 (0%) respectively in the age groups 21-40 years.

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Moreover, maximum cases 10 (9.61 %) with HbA1c ≤5.9% followed by ≥8.0 %, 6.0-6.9 % and 7-7.9 % with 8 (7.69 %), 7 (6.73 %) and 5 (4.8 %) respectively in the age groups 61-80 years. Out of 104 cases, 51 (49.04 %) were male and 53 (50.96 %) were female.

Table 1. Distribution of Frequency of glycemic control in Type 2 DM patients (n=104).

Age Groups	Glycemic Control (HbA1c %)	Male (%)	Female (%)	Total (%)
21-40	≤5.9 %	4 (3.84)	5 (4.80)	9 (8.65)
	6.0-6.9 %	0 (0)	1 (0.96)	1 (0.96)
	7.0-7.9 %	0 (0)	0 (0)	0 (0)
	≥8.0 %	4 (3.84)	4 (3.84)	8 (7.69)
41-60	≤5.9 %	8 (7.69)	7 (6.73)	15 (14.42)
	6.0-6.9 %	7 (6.73)	7 (6.73)	14 (13.46)
	7.0-7.9 %	2 (1.92)	4 (3.84)	6 (5.76)
	≥8.0 %	10 (9.61)	11 (10.57)	21 (20.19)
61-80	≤5.9 %	4 (3.84)	6 (5.76)	10 (9.61)
	6.0-6.9 %	6 (5.76)	1 (0.96)	7 (6.73)
	7.0-7.9 %	1 (0.96)	4 (3.84)	5 (4.80)
	≥8.0 %	5 (4.80)	3 (2.88)	8 (7.69)
Total		51 (49.04)	53 (50.96)	104 (100)

Table 2 represents the distribution of Mean ± SD according to FBS, PPBS, HbA1c and eAG where the maximum cases fall in the age group 41-60 years with frequency 56 (53.84 %) comprising 27 (25.96 %) male and 29 (27.88 %) female respectively. It is followed by age group 61-80 year and 21-40 year with frequency of cases 30 (28.84 %) and 18 (17.3 %) respectively. The mean & SD of HbA1c% (7.6 ± 2.9 %) and eAG (172.66 ± 81.79 mg/dl) were found to be maximum in the age group 41-60 years followed by 21-40 years and 61-80 years respectively.

Table 2. Age and Sex wise distribution of Mean ± SD of FBS, PPBS, HbA1c and eAG (n=104).

Age Groups	Sex	Age	FBS mg/dl	PPBS mg/dl	HbA1c %	eAG (mg/dl) 28.7XHbA1c%-46.7
21-40	M(n=8)	34.13 ± 6.77	178.75 ± 82.74	261.0 ± 93.18	7.5 ± 3.8	168.37 ± 107.84
	F (n=10)	36.30 ± 3.68	171.9 ± 79.74	248.5 ± 99.45	7.4 ± 3.2	165.88 ± 92.82
	18	35.21 ± 5.21	175.32 ± 81.24	254.75 ± 96.31	7.5 ± 3.5	167.12 ± 100.33
41-60	M(n=27)	53.70 ± 5.23	159.15 ± 62.14	240.22 ± 90.34	7.3 ± 2.6	162.0 ± 75.40
	F(n=29)	51.55 ± 6.06	168.65 ± 56.53	255.86 ± 86.39	8.0 ± 3.1	183.32 ± 88.18
	56	55.12 ± 5.64	163.9 ± 59.33	248.04 ± 88.36	7.6 ± 2.9	172.66 ± 81.79
61-80	M(n=16)	70.63 ± 6.35	156.0 ± 53.10	214.69 ± 84.37	7.1 ± 2.2	157.29 ± 62.61
	F(n=14)	68.35 ± 6.04	139.28 ± 59.01	216.71 ± 99.54	6.7 ± 2.4	142.47 ± 68.82
	30	69.49 ± 6.19	147.64 ± 56.02	215.7 ± 91.95	6.9 ± 2.3	149.88 ± 65.71
Total	M(n=51)	53.69 ± 16.23	158.29 ± 62.28	230.80 ± 89.57	7.1 ± 2.7	159.11 ± 74.37

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	F(n=53)	51.10 ± 14.93	158.54 ± 62.51	239.11 ± 93.16	7.4 ± 3.0	166.67 ± 82.92
	104	52.39 ± 15.58	158.41 ± 62.39	234.95 ± 91.36	7.3 ±2.9	162.89 ± 78.64

Table 3. Correlation of HbA1c/eAG with FBS & PPBS.

Patients	Variables	HbA1c/eAG
Male	FBS	+0.65
	PPBS	+0.67
Female	FBS	+0.77
	PPBS	+0.77
Total	FBS	+0.71
	PPBS	+0.73

Table 3 shows the correlation of glucose level with HbA1c/eAG. There were statistically significant positive correlation was observed between FBS, PPBS with HbA1c/eAG (*p<0.001*).

DISCUSSION

Long term complications of T2DM include retinopathy, nephropathy, peripheral and autonomic neuropathy and cardiovascular diseases cause huge medical and socioeconomic burden on the society and impose enormous strains on health care systems[8]. Our study has shown the maximum frequency (20.19 %) of patients were in the category of bad glycemic control HbA1c%≥8 % in age group 41-60 years. The overall frequency of female (50.96 %) was more than that of male (49.04 %) which was statistically insignificant. The eAG level of chronic glycemia, as determined by measurements of glycosylated hemoglobin, may also be an independent risk factor for coronary artery disease, particularly in women[9].

The mean & SD of HbA1c% (7.6 ± 2.9 %) and eAG (172.66 ± 81.79 mg/dl) were found to be maximum in the age group 41-60 years. This indicates the most vulnerable age group was 41-60 years with abnormal glycemic control. Moreover, there was significant positive Pearson's correlation has been shown between FBS/PPBS with HbA1c/eAG in type 2 Diabetes patients indicating the level of HbA1c can increase or decrease relatively quickly with large changes in glucose. It does not take 120 days to detect a clinically meaningful change in HbA1c following a clinically significant change in average glucose. Moreover, Fasting glucose should be used with caution as a surrogate measure of average glucose. HbA1c is a more comprehensive measure of total glycemic exposure than FPG due to the representation of blood glucose in the postprandial state in addition to the fasting state[10]. HbA1c is a weighted average of glucose levels during the preceding 4 months. Hence, unless the patient's glucose levels are very stable month after month, quarterly measurement is needed to insure that a patient's glycemic control remains within the target range. Although the American Diabetes Association (ADA) does not currently recommend HbA1c measurement for the diagnosis of diabetes, studies have shown frequency distributions similar to those of fasting plasma glucose (FPG) used in diagnosing diabetes[11].

The measurement of glycated hemoglobin is central to good-quality diabetes care. This is a measure by which healthcare providers can relate blood glucose control to the risk of complications. The working group by International Diabetes Federation (IDF) was established to develop a standard and harmonise HbA1c reporting[12]. Diabetes mellitus patients with abnormal glycemic control are associated with microvascular complication[10], macrovascular complications[13], cardiovascular disease[13] and positive correlations with metabolic syndrome are also suggested[14]. The clinician decides if a patient has achieved glycemic control, and, therefore, determines all resulting therapeutic actions based on the interpretation of a single determination of the blood levels of HbA1c or eAG[15]. In this study, type 2 DM has been seen with increased HbA1c with poor glycemic control in all age groups and observed significantly direct association with FBS, PPBG and eAG respectively.

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