Research Article (Open access)

Role of Glycated Hemoglobin in the Diagnosis of Diabetes Mellitus and Pre-diabetes

Naresh Kumar Jha*
Department of Biochemistry, Lord Buddha Koshi Medical College, Saharsa, Bihar, India

*Address for Correspondence: Dr. Naresh Kumar Jha, Associate Professor, Department of Biochemistry, Lord Buddha Koshi Medical College, Saharsa, Bihar, India

Received: 05 December 2016/Revised: 21 December 2016/Accepted: 12 January 2017

ABSTRACT

Background: Importance of measurement of glycated hemoglobin (HbA1c) has been recommended for the diagnosis of diabetes and pre-diabetes. However, various epidemiological studies conducted in different parts of the universe have shown significant discordance between HbA1c and glucose-based tests. HbA1c is assumed to be the gold standard for monitoring glycemic control in patients with diabetes mellitus disorder. HbA1c assay provided an accurate, precise measure of chronic glycemic levels and associates with the risk of diabetes complications.

Methods: This was a cross-sectional, prospective study. A total of 868 individuals attended to the medicine outpatient clinic at Lord Buddha Koshi Medical College, Saharsa, Bihar between Jan 2016 to Dec 2016 for the study after screening a large cohort visited OPD. The results of FPG, Oral glucose tolerance test (OGTT), and HbA1c for 868 individuals were analyzed as well as all grouped as diabetic patients, glucose intolerant (pre-diabetes) patients, and non-diabetic patients according to the new American Diabetes Association (ADA) criteria for the diagnosed of diabetes.

Results: Diagnostic sensitivity of all diabetic criteria was 80.33% for A1c; 75% for OGTT and only 41.87% of FPG, respectively.

Conclusion: The proposed A1c diagnostic criteria had greater diagnostic than FPG and 2-h OGTT regards a diagnosis of diabetes mellitus disorder.

Key-words- Diabetes Mellitus, Fasting Plasma Glucose, Glycated Hemoglobin, Oral glucose tolerances test (OGTT), Pre- diabetes

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INTRODUCTION

Glycated hemoglobin (HbA1c) has been recommended for the diagnosis of diabetes and pre-diabetes these days. However, various epidemiological studies conducted different parts of the universe have shown significant discordance between HbA1c and glucose-based tests. Some factors that could influence agreement between HbA1c and OGTT, body weight have not been fully evaluated.

Glycated hemoglobin (HbA1c) is assumed to be the gold standard for monitoring glycemic control in patients with diabetes mellitus.

Access this article online	
Quick Response Code	Website: www.ijlssr.com
	crossref DOI: 10.21276/ijlssr.2017.3.2.1

HbA1c evaluates an accurate, accurate measure of chronic glycemic levels and associates with the risk of diabetes complications.

The purpose and utility of this test has been extended to diagnose and screen for diabetes mellitus with the endorsement of several international diabetes societies and the World Health Organization. In 2010, the International Expert Committee and the American Diabetes Association postulated diagnostic criteria for diabetes and prediabetes based on HbA1c levels. These are HbA1c ≥6.5% (≥48 mmol/mol) to diagnose diabetes mellitus and between 5.7–6.4% (39–46 mmol/mol) for prediabetes [1]. Since the recommendation of the International Expert Committee in 2009 to use HbA1c test to diagnose diabetes [3], the Endocrin Society [5], the World Health Organization [6], and most scientists in different countries all over the world have endorsed using HbA1c to diagnose diabetes.

Epidemiological studies have shown significant between HbA1c and glucose-based tests for defining diabetes and pre-diabetes. The diagnosis of diabetes, HbA1c showed 24% sensitivity and 99% specificity [2]. These levels of sen-

sitivity and specificity were replicated in several other studies [3–7], all suggesting the poor agreement between HbA1c, fasting plasma glucose (FPG) and 2-h plasma glucose (2 h PG).

therefore more , diagnostic agreement of HbA1c criteria with the fasting and 2 h glucose-based criteria for pre-diabetes was also questioned [8,9], and might be different across ethnic groups and populations[10], thus suggesting that the diagnostic performance of HbA1c will depend also on the target population. In the study by Mann [8], for example- pre-diabetes by the HbA1c criterion showed 27% sensitivity and 93% specificity, with 61% positive predictive value, a result confirmed by Heinaza [9], everywhere a threshold of HbA1c 5.7% again showed low sensitivity (24%) with high specificity (91%), whereas HbA1c of 5.5% gave the highest combination of specificity (76%) and sensitivity (46%).

Obesity is one of the most important risk factors for diabetes and impaired glucose regulation [11], It might be postulated that in obese subjects, at increased risk for glucose abnormalities, the efficacy of HbA1c could be higher than in normal weight people, and therefore of increased clinical utility. One current study has shown a modest increased risk of prediabetes linked with obesity [12]. Some exist our knowledge; no studies have explored the impact of different grades of obesity (class I–III) on the efficacy of HbA1c to diagnose diabetes and prediabetes.

Last decades some studied were showed that the large population of patients that are discordantly categorized by HbA1c or OGTT; their phenotypic characterization needs to be assessed, in order to identify those parameters that could be of help in the choice of the most appropriate diagnostic tests.

Finally, in last decades studied [13] so far has analyzed that the association between HbA1c and plasma glucose values for the diagnosis of prediabetes, showing again poor agreement between HbA1c and FPG.

Past study HbA1c can be used as a dual marker of hyperglycemia and dyslipidemia in type 2 diabetes mellitus [14]. Improving glycemic control can substantially reduce the risk of cardiovascular events in diabetics [15]. Cholesterol, saturated fats and excessive amounts of sodium have been identified as factors of high blood pressure and Cardiovascular disease [16]. Other factors play a similarly important role, if not more, in the pathogenesis of diabetic complications, oxidative stress plays a significant role in diabetes and its complications [17]. The alteration function of endothelium along with antioxidant/pro-oxidant imbalance in hypertension can lead to detrimental consequences and long-term adverse effects of atherosclerosis and cardiovascular disease [18]. Past study shown between antioxidant nutrient intake and decrease in the development of diabetic complications [19]. Vitamin C may be helpful in decreasing blood glucose type 2 diabetes and thus reducing the risk of complications [20].

Hence, the aims of the current study were to evaluate the impact of HbA1c criteria to diagnose diabetes and pre-diabetes in two large cohorts of participants undergoing OGTT. Then, we aimed to investigate whether differences exist between obesity classes I–III with respect to the relationship of HbA1c and blood glucose. Finally, we examined who had a diagnosis of prediabetes with the OGTT, but had a normal HbA1c, comparing them with those that were concordant with both tests, consider to might most appropriate diagnostic test.

MATERIALS AND METHODS

This is a cross sectional, prospective study. A total of 868 individuals attended to the medicine outpatient clinic between Jan 2016 to Dec 2016 were selected for the study after screening a large cohort visited OPD. The results of FPG, OGTT and HbA1c for 868 individuals were analyzed and all grouped as diabetic patients, glucose intolerant (pre-diabetes) patients and non-diabetic patients according to new ADA criteria for the diagnosis of diabetes.

Inclusion Criterion- Only those with concurrent FPG, OGTT, and A1c results and diabetes mellitus suspicion were included. OGTT is routinely obtained in our hospital, if there is a suspicion of diabetes mellitus.

Exclusion Criterion- Diabetic subjected and patients, who had been using drugs associated with the development of diabetes, were excluded.

The study group consisted of 348 males (40%) and 520 females (60%). Mean age of the subjects was 57.3±18.6 yr.

FPG, OGTT, A1c levels of subjects were measured with the help of central laboratory & department of Biochemistry. All individual subjects (*n* =868) were grouped as diabetic patients, glucose intolerant (pre-diabetes) patients, and non-diabetic patients according to new ADA criteria for the diagnosis of diabetes disorder. The current diagnostic criteria proposed by the American Diabetes Association (ADA) for diabetes are A1c ≥6.5%, FPG ≥126 mg/dl (7.0 mmol/l), 2nd h plasma glucose ≥200 mg/dl (11.1 mmol/l) during the OGTT in the patients with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dl (11.1 mmol/l). IFG was defined as a FPG with 100 mg/dl (5.6 mmol/l)–125 mg/dl (6.9 mmol/l). IGT was defined as 2-h glucose with 140 mg/dl (7.8 mmol/l)-199 mg/dl (11.0 mmol/l) or A1c values between 5.7% and 6.4%.

Performance of FPG, OGTT, and A1c tests were done with the following steps:

1. **FPG**: After 12 h fasting period, blood samples were drawn by standard phlebotomy into regular blood (serum) test-tubes between 8:00 AM and 10:00 AM and serum glucose level was measured by an enzymatic method (hexokinase).
2. **OGTT:** All subjects were informed to take at least 150 g of carbohydrate each day for at least 3 days before this test. After 12h fasting period, 75g of glucose was given to each individual to ingest in the form of a cool drink.

3. Blood samples were taken by standard phlebotomy into regular blood (serum) test tubes at time 0 and 120 min by a health- care provider.
4. **HbA1C:** Blood samples were obtained by standard phlebotomy into ethylene diamine tetra acetic acid-containing tubes by Nephelometry method was used in the analysis of HbA1c.

STATISTICAL ANALYSIS

All results were shown as a mean±standard deviation. The *p* values were based on the two- side tests with a cut off for statistical significance of 0.05. The Chi-square test, Kol-mogorov-Smirnov test, and Analysis of co-variance test were used to evaluate values. All statistical analyses were performed with SPSS version 20.0.

RESULTS AND DISCUSSION

The present study showed the poor agreement between HbA1c, FPG, and 2-h glucose post OGTT for the diagnosis of Diabetes Mellitus and Pre-diabetes. This investigation compared between FPG and HbA1C rapid tests in identify-ing diabetes and pre-diabetes when used in a screening strategy among 35–74 year old persons.

Therefore, HbA1c could reproduce a mishmash of the patho-physiological defects underlying IFG and IGT over time. In fact, we examined the highest concordance with HbA1c when the two conditions of IFG + IGT were present together.

According to new ADA criteria; we were determined 480 diabetic patients among the 868 individuals (55.3%). However, 96 diabetic patients (20.0%) met all ADA crite-ria. All results are shown in Table 1 & Table 2. Total 388 diabetic patients (80.83%) were diagnosed by A1c alone, 360 diabetic patients (75%) with 2-h OGTT alone, and 201 (41.87 %) diabetic patients were diagnosed with FPG alone (Table 2). Differences between FPG versus 2-h OGTT, FPG versus As1c and OGTT versus A1c were statistically significant (p <0.05, p <0.05, and p<0.05, respectively). Diagnostic sensitivity of all diabetic criteria found 80.33% for As1c; 75% for OGTT, and only 41.87% of FPG respec-tively.

Table 1: Frequency of individuals and distribution of mean FPG, 2-h OGTT and HbA1c values of the diabetic patients and non-diabetic individuals according to age groups

Age Group	Gender		Total	Test	Non Diabetic Patients	Diabetic Patients	All individuals
	Male	Female					
≤45 yrs	80	101	181	FPG	112±32	148±61	96±12
				2-HOGTT	149±82	232±112	139±31
				HbA1c	6.11±1.37	7.98±1.72	5.01±0.88
45-60 yrs	154	206	366	FPG	115±41	138±51	91±19
				2-HOGTT	149±71	232±89	132±21
				HbA1c	5.81±1.41	7.08±1.02	6.01±0.28
60 & Above	122	199	321	FPG	118±30	158±68	86±19
				2-HOGTT	165±80	252±119	131±39
				HbA1c	5.31±1.27	8.98±1.62	5.31±0.81

FPG= Fasting Pasma glucose, OGTT= Oral glucose tolerance test, HbA1c = glycated hemoglobin

Table 2: Pre-diabetes and diabetes frequencies

S. No	Diagonostic criterion	Positive	Negatiave	Total	p-value
	FPG	201	279	480	p<0.05
1	2-hOGTT	360	120	480	
	HbA1c	388	92	480	
	IFG	304	176	480	
	IGT 2-h OGTT	86	394	480	p<0.05
2	IGTHbA1c	123	357	480	
	IFG	154	326	480	
3	IGT 2-h OGTT	170	698	868	p<0.05
	IGT HbA1c	401	467	868	

1. Results according to new ADA Criterion, 2. Frequencies of imparied fasting glucose & imparied glucose tolerence (2-h OGTT & HbA1c), 3. Frequency of impaired fasting glucose & imparied glucose tolerence (2-h OGTT & A1c) among diabetic patients
FPG= Fasting plasma glucose, OGTT= Oral glucose tolerance test, IFG = Impaired fasting glucose, IGT = Impaired glucose tolerance

IFG and glucose intolerance utility- According to new ADA criteria, of the 868 subjects tested, 1094 (60.3%) were classified as having IFG, 154 (32.08%) as having IGT following OGTT and 401 (46.01%) as having IGT by A1c. In terms of a diagnostic ratio of glucose intolerance; the difference between A1c and OGTT was statistically significant ($p< 0.05$) (Table 2 & Table 3).

Table 3: Distribution of all diabetic patients according to FPG, 2-H OGTT and HbA1c

	Fasting Plasma Glucose mg/dL		Total	2-h OGTT mg/dL			Total
	<126	≥126		<140	140-200	≥ 200	
A1C <6.5	336	154	490	313	217	98	628
A1C <6.5	267	111	378	101	88	51	240
Total	603	265	868	530	305	149	868

CONCLUSIONS

By using $A1_C$ as a marker of diabetes criterion would re-classify the diabetes diagnosis. It is suggested that clinicians and health systems understand the differences and similarities by using A1c or FPG and 2-h OGTT in the diagnosis of diabetes mellitus and pre-diabetes. The proposed A1c diagnostic criteria have greater diagnostic than FPG and 2-h OGTT regards the diagnosis of diabetes mellitus.

REFERENCES

[1] American Diabetes Association. Standards of medical care in diabetes. Diabetes Care, 2013; 36(Suppl. 1): S11–S66.

[2] Van't Riet E, Alssema M, Rijkelijkhuizen JM. Relationship between A1C and glucose levels in the general Dutch population: the new Hoorn study. Diabetes Care, 2010; 33: 61–66.

[3] Cowie CC, Rust KF, Byrd-Holt DD. Prevalence of diabetes and impaired fasting glucose in adults in the U.S. population: National Health Nutrition Examination Survey 1999–2002. Diabetes Care, 2006; 29: 1263–68.

[4] Zemlin AE, Matsha TE, Hassan MS. HbA1c of 6.5% to diagnose diabetes mellitus–does it work for us? the Bellville South Africa study. PLoS One, 2011; 6: e22558.

[5] Cavagnolli G, Comerlato J, Comerlato C. HbA (1c) measurement for the diagnosis of diabetes: is it enough? Diabet Med., 2011; 28: 31–35.

[6] Buell C, Kermah D, Davidson MB. Utility of HbA1c for diabetes screening in the 1999 2004 NHANES population. Diabetes Care, 2007; 30: 2233–35.

[7] Tanaka Y, Atsumi Y, Matsuoka K. Usefulness of stable HbA1c for supportive marker to diagnose diabetes mellitus in Japanese subjects. Diabetes Res. Clin. Pract., 2001; 53: 41–45.

[8] Mann DM, Carson AP, Shimbo D. Impact of A1C screening criterion on the diagnosis of pre-diabetes among U.S. adults. Diabetes Care, 2010; 33:2190–95.

[9] Heianza Y, Hara S, Arase Y. HbA1c 5.7–6.4% and impaired fasting plasma glucose for diagnosis of prediabetes and risk of progression to diabetes in Japan (Topics 3): A longitudinal cohort study. Lancet, 2011; 9: 147–55.

[10] Ziemer DC, Kolm P, Weintraub WS. Glucose-independent, Black- White differences in hemoglobin A1c levels. Ann. Intern. Med., 2010; 152:770–77.

[11] Chen L, Magliano DJ, Zimmet PZ. The worldwide epidemiology of type 2 diabetes mellitus-present and future perspectives. Nat Rev Endocrinol., 2011; 8: 228–36.

[12] Buckley CM, Madden J, Balanda K. Pre-diabetes in adults 45 years and over in Ireland: the Survey of Lifestyle, Attitudes and Nutrition in Ireland 2007. Diabet Med., 2013; 30: 1198–103.

[13] Marini MA, Succurro E, Castaldo E. Cardiometabolic risk profiles and carotid atherosclerosis in individuals with prediabetes identified by fasting glucose, post challenge glucose, hemoglobin A1c criteria. Diabetes Care, 2012; 35: 1144–49.

[14] Alam R, Verma MK, Verma P. Glycated Hemoglobin as a Dual Biomarker in Type 2Diabetes Mellitus Predicting Glycemic Control and Dyslipidemia Risk. Int. J. Life Sci. Scienti. Res., 2015; 1(2): 62-65.

[15] Tripathi GK, Sharma R, Verma MK, Sharma P, Kumar P. Biomarkers in Serum Uric Acid as a Risk Factor for Type 2 Diabetes Associated with Hypertension. Asian. J. Pharm. Clin. Res., 2016; 9(2): 352-55.

[16] Verma M, Verma P, Parveen S, Dubey K. Comparative Study of Lipid Profile Levels in Vegetarian and Non-Vegetarian Person. Int. J. Life Sci. Scienti. Res., 2015; 1(2): 89-93.

[17] Verma MK, Singh SP, Alam R, Verma P. Comparative Study on MDA, SOD and HbA1c Levels in Patients Of Type 2 Diabetes Mellitus With Retinopathy and Without Retinopathy. Int. J. Pharm. Sci. Res., 2016; 7(10): 4184-90.

[18] Singh SP, Verma MK, Tripathi P, Singh D. Comparative Study of Malondialdehyde and Vitamin C in Type 2 Diabetes Mellitus and Non Diabetic Individuals. Int. J. Life Sci. Scienti. Res., 2016; 2(1): 31-36.

[19] Verma M, Alam R, Mobin M. Review on Malondialdehyde and Superoxide dismutase levels in patients of Type 2 Diabetes Mellitus with Retinopathy and without Retinopathy. Int. J. Life Sci. Scienti. Res., 2015; 1(2): 52-57.

[20] Tripathi P, Verma MK, Tripathi SS, Singh SP. Comparative Study of Malondialdehyde and Vitamin C in Type 2 Diabetes Mellitus and Non Diabetic Individuals. Int. J. Life Sci. Scienti. Res., 2016; 2(1): 09-14.

How to cite this article:
Jha NK: Role of Glycated Hemoglobin in the Diagnosis of Diabetes Mellitus and Pre-diabetes. Int. J. Life Sci. Scienti. Res., 2017; 3(2): 882-886. DOI:10.21276/ijlssr.2017.3.2.1
Source of Financial Support: Nil, **Conflict of interest:** Nil

