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ORIGINAL ARTICLE

Relationship of HbA1C to blood glucose concentrations in children with type 1 diabetes mellitus from Eastern India

Prashant Manohar Gaikwad[1] · Deep Hathi[1] · Soumik Goswami[1] · Nilanjan Sengupta[1] · Arjun Baidya[1] · Niladri Das[1]

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Abstract

Background Racial and ethnic differences in HbA1c have been recognized for many years.

Objective The objective of this study is to find out the correlation between HbA1C and mean glucose levels in children diagnosed with type 1 diabetes mellitus from Eastern India.

Methods Thirty patients who aged 4–18 years with type 1 diabetes mellitus were included. Ambulatory glucose profile(AGP) was obtained with Abbott Freestyle Libre Pro over 2 weeks and was followed by 5 point CBG monitoring done by glucose meter (pre-breakfast, 2 h post breakfast, 2 h post lunch, pre-dinner, 2 h post dinner) for the next 2 weeks. The same protocol repeated for the 2 subsequent months to obtain average glucose levels for a 12 week period. HbA1C was tested at the end of the 12 week period by HPLC method. The relationship between HbA1C and mean blood glucose was determined by Pearson's correlation coefficient.

Results The coefficient of correlation was 0.923 for average glucose and HbA1c in study which was 0.922 in ADAG study. We found that at lower glucose levels Indian patients had low HbA1c levels compared to ADAG study group while the opposite was seen at higher glucose levels.

Conclusion Although the correlation between HbA1C and average glucose is similar between Indians and ADAG study population, the average blood glucose level for a given HbA1c is significantly different between them.

Keywords Glycated hemoglobin · HbA1c · Average glucose · Eastern India · ADAG

Abbreviations

HbA1C	Hemoglobin A1c
AGP	Ambulatory glucose profile
ADAG	A1c derived average glucose

✉ Prashant Manohar Gaikwad
prashantgaikwad6690.pg@gmail.com

Deep Hathi
deephathi18@gmail.com

Soumik Goswami
dr.soumikgoswami@gmail.com

Nilanjan Sengupta
drnilanjansengupta@gmail.com

Arjun Baidya
arjun.baidya@gmail.com

Niladri Das
niladrimedmamc@gmail.com

[1] Department of Endocrinology, NRS Medical College Kolkata, NL 1A, Building No, 17, Room no. 8 Sector-10 Nerul, Navi Mumbai, Maharashtra 400706, India

Introduction

In late 1960, hemoglobin A1 was recognized as a hemoglobin in the glycated form and found to be increased in patients with diabetes mellitus [1], and in 1976 hemoglobin A1c (HbA1c) was proposed as an indicator glucose regulation in diabetes mellitus. HbA1c is used as an index of glycemic control in patients with diabetes mellitus, correlates with risk for the development complications of diabetes mellitus [2, 3] . In 2009, American Diabetes Association (ADA), the European Association for the Study of Diabetes, and the International Diabetes Federation recommended the use of HbA1c for diagnosis of diabetes as one of the criteria [4] . In 2010, the ADA recommended HbA1c of 6.5% for the diagnosis of diabetes mellitus, using a method certified by the National Glycohemoglobin Standardization Program [5] .

For many years, it is known that there is racial and ethnic difference in HbA1c. The data derived from National Health and Nutrition Examination Survey from the 1999 to 2000 and analyzed by Boltri et al. mainly involving undiagnosed and diagnosed diabetes patients of different

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ethnicity, evaluated for HbA1c. Mean HbA1c was 7.6% in Whites, mean HbA1c was 8.2% in Hispanics and it was 8.1% in Blacks [6]. Cohort of participants were further followed from the 1999–2002 by Saydah et al. and analyzed data, found that differences in HbA1C for race/ethnicity was persistent [7].

The Third National Health and Nutrition Examination Survey (NHANES-3) involved participants aged 5 to 24 years who were non diabetic, Saaddine et al. analyzed data and found that non-Hispanic Black youths had high HbA1c levels than non-Hispanic Whites, Hispanic-Americans [8]. Eldeirawi and Lipton et al. in a study found that African-Americans, Mexican- Americans had high mean HbA1c levels as compared to non-Hispanic Whites [9].

Studies involving comparison of HbA1c between non-U.S. populations for ethnic variation are scarce but it is found that nondiabetic levels of HbA1c in some groups for example black Brazilians, South Asians population are higher compared with Whites [10–12].The causes for racial differences in HbA1c are differences of diet, lifestyle,body composition, physical activity, stress, and environmental factors that affect circulating non-fasting glucose levels [13].

There is an absence of published data in Indian population in this area. We therefore sought to determine whether there are differences that are clinically meaningful in how A1C correlates to average plasma glucose in type 1 diabetes mellitus children from Eastern India.

Methods

Study design

This prospective, single centre pilot study was done in a tertiary care centre in Kolkata, India, over a duration of 18 months. Thirty patients diagnosed with type 1 diabetes mellitus between 4–18 years of age were included in our study. Patients having hemoglobinopathies or anemia, severe hypoglycemia or diabetic ketoacidosis, pregnant female, patients receiving glucocorticoid therapy were excluded.

Ambulatory glucose profile was obtained with Abbott Freestyle Libre Pro over 2 weeks and was followed by 5 point CBG monitoring done by glucose meter (pre-breakfast, 2 h postprandial after breakfast, 2 h postprandial after lunch, pre-dinner, 2 h postprandial after dinner) for the next 2 weeks. The same protocol repeated for the 2 subsequent months to obtain average glucose levels for a 12 week period. HbA1C was tested after 12 weeks from enrollment in the study by HPLC method (Fig. 1).

Statistical analysis

Linear regression model was applied to estimate Pearson's correlation coefficient to find out the correlation between HbA1C and mean glucose. The derived equation reflecting the linear relationship was used to calculate average glucose values for different HbA1c levels (Fig. 2). Data was analyzed using Microsoft Excel 2019 version.

Results

In our study, 29 patients were considered for final statistical analysis as one patient was lost to follow up. Mean average glucose was 210 mg/dl with standard deviation of 68.35 and average HbA1c value was 9.4% with standard deviation of 2.80. The Pearson's correlation coefficient for average glucose and HbA1c was 0.923 which was statistically significant. The linear relationship equation was derived $y = 27.477x—1.215$, where y is average glucose and x is HbA1c (Fig. 2). Estimated glucose values were determined at different HbA1c levels using this equation as depicted in Table 1. There was difference ($p = 0.034$) in the average glucose levels for HbA1C value, between our population and the ADAG population Table 2. We found that at lower glucose levels Indian children had lower HbA1c levels compared to ADAG study group while the opposite was seen at higher glucose levels [14].

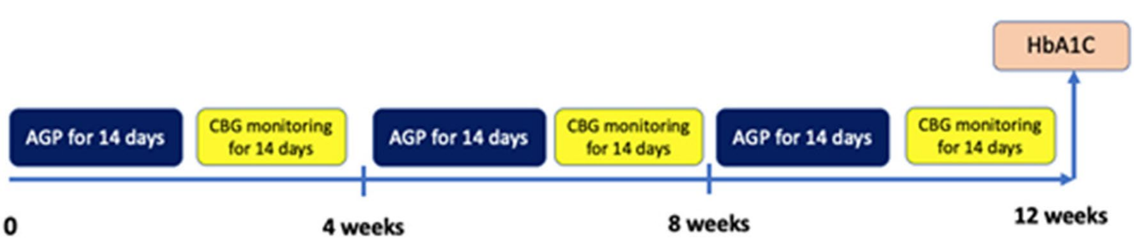

Fig. 1 Study protocol

Discussion

The coefficient of correlation for average glucose and HbA1c in present study was 0.923 (Table 3) which was very similar to that of ADAG study which was 0.922 [14]. However, there was a significant difference in the average glucose values for a given HbA1C between the 2 populations.

Our findings of racial difference between Indian population as compared to ADAG study population was similar to data analyzed by Boltri et al. from the 1999–2000 in National Health and Nutrition Examination Survey and found that Blacks have higher HbA1c as compared to Whites [6] while other studies have shown south Asians to have higher HbA1c as compared to Caucasians [10–12]. Our findings were consistent with to those of Saaddine et al. who analyzed HbA1c data for participants aged 5 to 24 years who were nondiabetic and concluded that non-Hispanic Black youths had high HbA1c levels compared to non-Hispanic Whites [8].

In this study, the discordance in the relationship between HbA1c and average blood glucose at low and high glucose levels can be explained by small sample size as only

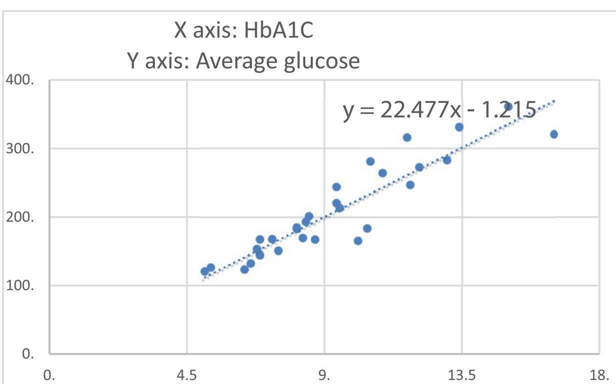

Fig. 2 Equation derived from linear regression model

Table 1 Derived average glucose value for corresponding HbA1C in this study and ADAG study

HbA1c	Estimated average glucose this study	Estimated average glucose ADAG study
5	111.17	97
6	133.64	126
7	156.12	154
8	178.6	183
9	201	212
10	223.55	240
11	246	269
12	268.5	298

Table 2 Paired t test for average glucose in ADAG study and this study

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	AVG glucose	210.0690	29	68.35022	12.69232
	ADAG AVG	223.17	29	80.619	14.971

Paired Samples Correlations

		N	Correlation	Sig
Pair 1	AVG glucose & ADAG AVG	29	0.922	0.000

Paired Samples Test

		Paired Differences					T	Df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	AVG glucose—ADAG AVG	−13.10345	31.71356	5.88906	−25.16664	−1.04026	−2.225	28	0.034

Table 3 Pearson correlation between HbA1C and average glucose

		Mean	Std. Deviation	N
AVG glucose		210.0690	68.35022	29
LAB HbA1C		9.400	2.8052	29
Correlations				
			AVG glucose	LAB HbA1C
AVG glucose	Pearson Correlation		1	0.923**
	Sig. (2-tailed)			0.000
	N		29	29
LAB HbA1C	Pearson Correlation		0.923**	1
	Sig. (2-tailed)		0.000	
	N		29	29

** Correlation is significant at the 0.01 level (2-tailed)

2 patients had HbA1c between 5–6%, 5 patients had HbA1c between 6–7% and only one patient had HbA1c between 7–8%. Hence there is a need for a study with larger sample size including patients with diabetes and normal individuals without diabetes to determine the relationship even at low or normal blood glucose levels.

This is the first study done in India to determine correlation between average glucose and HbA1c and to estimate differences in HbA1c as compared to ADAG study group. ADAG study had not included Asian population and children in study [14], this study included participants aged 4–18 years from India. The clinical and practical implication of this study, we may need race/ethnicity specific cutoff for diagnosis of diabetes mellitus and HbA1C treatment target, as the average blood glucose value for given HbA1C was different in this study population as compared to ADAG study population.

Conclusion

Although the correlation between HbA1C and average glucose is similar between Indians and ADAG study population, the average blood glucose level for a given HbA1c is significantly different between them.

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Declarations

Informed consent Informed consent was taken from patient's guardian

Conflict of interests The authors declare no conflict of interests.

References

1. Rahbar S. An abnormal hemoglobin in red cells of diabetics. Clin Chim Acta. 1968;22:296–8.
2. Koenig RJ, Peterson CM, Kilo C, Cerami A, Williamson JR. Hemoglobin A1c as an indicator of the degree of glucose intolerance in diabetes. Diabetes. 1976;25:230–2.
3. Koenig RJ, Peterson CM, Jones RL, Saudek C, Lehrman M, Cerami A. Correlation of glucose regulation and hemoglobin A1c in diabetes mellitus. N Engl J Med. 1976;295:417–20.
4. 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.
5. American Diabetes Association. Standards of medical care in diabetes—2010. Diabetes Care. 2010;33(Suppl 1):S11–61.
6. Boltri JM, Okosun IS, Davis-Smith M, Vogel RL. Hemoglobin A1c levels in diagnosed and undiagnosed Black, Hispanic, and White persons with diabetes: results from NHANES 1999–2000. Ethn Dis. 2005;15:562–7.
7. Saydah S, Cowie C, Eberhardt MS, De Rekeneire N, NarayanKMV,. Race and ethnic differences in glycemic control among adults with diagnosed diabetes in the United States. Ethn Dis. 2007;17:529–35.
8. Saaddine JB, Fagot-Campagna A, Rolka D, Narayan KM, Geiss L, Eberhardt M, Flegal KM. Distribution of HbA1c levels for children and young adults in the U.S. Diabetes Care. 2002;25:1326–30.
9. Eldeirawi K, Lipton RB. Predictors of hemoglobin A1c in a national sample of nondiabetic children. The Third National Health and Nutrition Examination Survey, 1988–1994. Am J Epidemiol. 2003;157:624–32.
10. Shipman KE, Jawad M, Sullivan KM, Ford C, Gama R. Ethnic/racial determinants of glycemic markers in a UK sample. Acta Diabetol. 2015;52:687–92.
11. de Miranda VA, Cruz Filho RA, de Oliveira TS, et al. Racial differences in HbA1c: a cross sectional analysis of a Brazilian public primary care population. Prim Care Diabetes. 2013;7:135–41.
12. Jørgensen ME, Bjerregaard P, Borch- Johnsen K, Witte D. New diagnostic criteria for diabetes: is the change from glucose to HbA1c possible in all populations? J Clin Endocrinol Metab. 2010;95:E333–6.
13. Selvin E. Are There Clinical Implications of Racial Differences in HbA1c? A Difference, to Be a Difference. Must Make a Difference Diabetes Care. 2016;39(8):1462–7. https://doi.org/10.2337/dc16-0042.
14. Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine RJ; A1c-Derived Average Glucose Study Group. Translating the A1C assay into estimated average glucose values. Diabetes Care. 2008 Aug;31(8):1473–8. https://doi.org/10.2337/dc08-0545. Epub 2008 Jun 7. Erratum in: Diabetes Care. 2009 Jan;32(1):207