Association between glycated hemoglobin A1c levels with age and gender in Chinese adults with no prior diagnosis of diabetes mellitus

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Abstract. The present cross-sectional study consisted of 18,265 Chinese patients not previously diagnosed with diabetes mellitus, and who underwent physical examination at the Third People's Hospital of Shenzhen between June 2014 and May 2015 (mean patient age, 51.312±15.252 years). The study was composed of 11,770 males and 6,495 females. The aim was to investigate the association between glycated hemoglobin A1c (HbA1c) levels, gender and age. HbA1c values were measured using a Bio-Rad VARIANT™ II HbA1c Reorder Pack. All data was collected for analysis of the HbA1c levels in different gender and age groups, in order to investigate the association between HbA1c levels and age. Analysis of the 18,265 total cases and 16,734 cases with HbA1c levels <6.5%, demonstrated a positive correlation between levels of HbA1c and patient age. Linear regression for patient age and HbA1c levels demonstrated that HbA1c (%) = 0.020 x age (years) + 4.523 (r=0.369, P<0.0001) and HbA1c (%) = 0.014 x age (years) + 4.659 (r=0.485, P<0.0001), respectively. HbA1c levels of the male group were significantly higher than those of the female group (P<0.0001). Furthermore, in different gender groups, HbA1c levels gradually rose with increasing age. Therefore, HbA1c levels are associated with age and gender in Chinese populations, and this should be considered when selecting HbA1c as a criterion for future diabetes screening.

Introduction

Glycated hemoglobin A1c (HbA1c) is a form of hemoglobin that is measured in order to identify the average concentration of plasma glucose over the relatively long-term period of two to three months prior to the date of measurement. Since HbA1c testing can be performed at any time of the day and without any special patient preparation (for example, fasting is not required) and provides more accurate information about the disease and the patient, it offers improved convenience for patients and health care providers compared to the oral glucose tolerance test or taking fasting plasma glucose measurements (1,2). On this basis, it has been suggested that HbA1c may serve as a better indicator for glucose control in diabetic patients than fasting blood sugar levels (3,4). Furthermore, HbA1c levels have been proposed as a diagnostic tool for identifying patients with undiagnosed diabetes or that have an elevated risk of developing diabetes (5). In 2011, the World Health Organization and the American Diabetic Association accepted HbA1c levels ≥6.5% as a diagnostic criterion for diabetes mellitus (6,7). However, it is important to take age, race/ethnicity, anemia/hemoglobinopathies (and other diseases for which HbA1c may be an unsatisfactory criterion for the diagnosis of type 2 diabetes) into consideration when using the HbA1c levels to diagnose diabetes (8-15). Further studies are thus required to promote a more appropriate standard for HbA1c in the diagnosis of type 2 diabetes. Furthermore, while HbA1c values have been previously reported to increase with age in Japanese patients (11), there are no reports about the association between HbA1c and gender and age in Chinese adults. In view of whether HbA1c levels may vary with the race or ethnicity of patients (16,17), the present study aims to evaluate the association between gender, age and HbA1c levels in Chinese adults that have not been diagnosed with diabetes mellitus.

Materials and methods

Study subjects. The present retrospective study comprised of 18,265 Chinese adults (aged 18-99 years, average age 51.312±15.252 years; 11,770 males, average age 52.892±15.445 years; 6,495 females, average age 48.449±14.466 years) who were not known to be suffering with diabetes and who underwent a comprehensive health examination between June 2014 and May 2015 at the Shenzhen Third People's Hospital (Shenzhen, China). The inclusion criteria for

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Table I. Comparison of HbA1c levels of different gender subjects.

Groups	All personnel		HbA1c <6.5% personnel		HbA1c ≥6.5% personnel	
	No.	HbA1c (%)	No.	HbA1c (%)	No.	HbA1c (%)
Male	11,770	5.619±0.894	10,542	5.385±0.446	1,228	7.621±1.212
Female	6,495	5.454±0.706	6,192	5.347±0.427	303	7.635±1.400
t-value	13.730		5.547		-0.178	
P-value	<0.0001		<0.0001		0.859	

All data are presented as the mean ± standard deviation or as number of participants; comparison of HbA1c levels between male and female was done with independent sample t-test. HbA1c, hemoglobin A1c.

the study was as follows: i) Han ethnicity; ii) age ≥18 years; iii) resident of mainland China for >1 year; and iv) no previous diagnosis of diabetes. Exclusion criteria was as follows: Previously known diabetes, pregnancy, heart/liver/kidney dysfunction, long-term oral administration of drugs affecting blood glucose, long-term history of smoking, anemia/hemoglobinopathies, and surgery within the past month (13,18). The age range of the participants was divided into seven groups: 18-29, 30-39, 40-49, 50-59, 60-69, 70-79 and ≥80 years. The study protocol was approved by the Ethics Committee of Shenzhen Third People's Hospital. All the participants included in the present study provided written informed consent.

Sample collection and measurement. A 2 ml venous blood sample was collected in the morning following 8-12 h of overnight fasting. Blood sample HbA1c levels were measured within 2 h using a high-performance liquid chromatography VARIANT™ II hemoglobin testing system (Bio-Rad Laboratories, Inc., Hercules, CA, USA). Detection was performed strictly in accordance with the manufacturer's instructions using the original kit, calibration, and quality control. The intra- and inter-assay coefficients of variation for HbA1c were both <0.8%. All procedures were carried out by trained doctors at Shenzhen Third People's Hospital.

Statistical analysis. All data are presented as the mean ± standard deviation (SD) for variables with normal distribution, the median (interquartile range) for variables with a non-normal distribution, or as the number of participants. One variable comparison between two groups was analysed using an independent sample t-test. Analysis of one-way ANOVA was first used in multiple groups comparison, and pairwise comparison in multiple groups was conducted using the LSD-T method. Correlation analysis among different variables was performed with Pearson correlation analysis and linear regression. A value of P<0.05 was considered to indicate a statistically significant difference. All statistical analysis was performed using the SPSS software, version 21.0 (IBM SPSS, Armonk, NY, USA).

Results

Comparison of HbA1c levels in males and females. As shown in Table I, there were significant differences (P<0.0001) in HbA1c levels between the male and female groups in the total study population (referred to all personnel) and the HbA1c <6.5% (referred to HbA1c <6.5% personnel). It specifically demonstrated that the overall levels of HbA1c were higher in male than that in female (Table I).

Comparison of HbA1c levels across different age groups. HbA1c test results for all age groups are shown in Table II and Fig. 1. The data suggested two interesting results: i) HbA1c values of all personnel and HbA1c <6.5% personnel, in both males and females, gradually increased with age until 79 years, and then plateaued (Fig. 1); ii) HbA1c levels of HbA1c ≥6.5% patients of either gender gradually decreased with age (Fig. 1). An independent sample t-test was performed on HbA1c levels for males and females of the same age group. The results showed that the difference of HbA1c values in different gender of 30-59 years old subjects was statistically significant (P<0.05), and male HbA1c levels were higher than those of females (Table II). The difference in HbA1c levels in different gender of the other four age-groups was not significant (P>0.05) (Table II).

Correlation between HbA1c levels and age. Linear regression analysis showed that HbA1c levels were positively correlated with age in all personnel (increase of 0.020% per decade) and HbA1c <6.5% personnel (increase of 0.014% per decade), the linear regression equations were HbA1c (%) = 0.020 x age (years) + 4.523 (r=0.369; P<0.0001) and HbA1c (%) = 0.014 x age (years) + 4.659 (r=0.485; P<0.0001), respectively. By contrast, HbA1c levels were negatively correlated with age in HbA1c ≥6.5% personnel (decreased 0.012% per decade), the linear regression equation was HbA1c (%) = -0.012 x age (years) + 8.345 (r=0.124; P<0.0001).

Discussion

The results of the current study suggest that greater attention should be given to patient gender and age when selecting HbA1c as the criterion in diabetes screening, as has been reported in previous studies (8,11,13,19-21). HbA1c levels, which were significantly higher in male than that in female and increased steadily as age rose, differ significantly by gender and age.

The HbA1c levels of male individuals were significantly higher than those of females in the 30-59 years age-groups (P<0.05). It is most likely due to factors such as blood pressure

Table II. Comparison of HbA1c levels of different age groups.

Age groups, years	All personnel		Male		Female		t-value	P-value
	No.	HbA1c (%)	No.	HbA1c (%)	No.	HbA1c (%)		
18-29	1,380	4.994±0.399	727	4.975±0.405	653	5.014±0.392	-1.829	0.068
30-39	2,697	5.180±0.605	1,566	5.221±0.681	1,131	5.123±0.473	4.392	<0.001
40-49	4,449	5.404±0.700	2,698	5.464±0.790	1,751	5.310±0.519	7.847	<0.001
50-59	4,905	5.695±0.881	3,308	5.718±0.949	1,597	5.646±0.718	2.954	0.003
60-69	2,329	5.852±0.853	1,548	5.875±0.897	781	5.807±0.759	1.914	0.056
70-79	1,499	6.019±0.950	1,144	6.031±0.958	355	5.981±0.924	0.885	0.377
≥80	1,006	6.028±0.858	779	6.015±0.826	227	6.072±0.959	-0.872	0.383

All data are presented as the mean ± standard deviation or as number of participants; comparison of HbA1c levels between male and female was done with independent sample t-test. HbA1c, hemoglobin A1c.
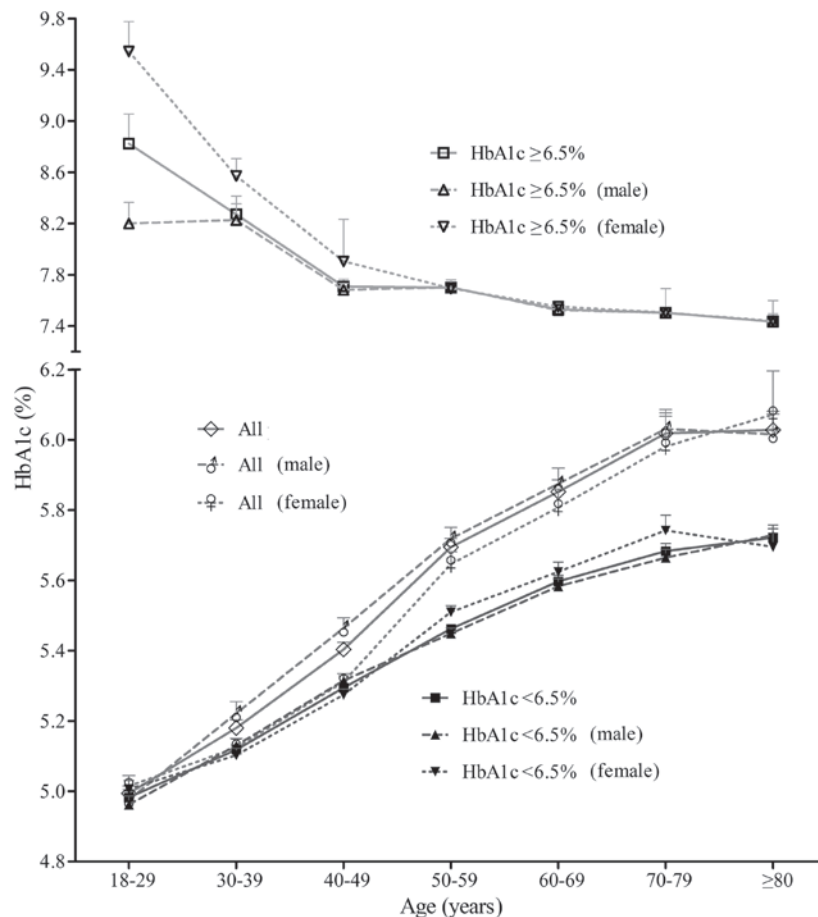

Figure 1. Hemoglobin A1c (HbA1c) levels in seven age categories. Error bars display 95% confidence intervals in each category.

and blood lipids of males in this age-group have worse control conditions, and women may be easily affected by physiological cycle. As in previous reports (19,22-24), gender differences were noted in the relationship between HbA1c and age. It is possible that this finding is related to lower hemoglobin levels in menstruating women with more rapid erythrocyte turnover, as suggested previously (19). Women in peri- and post-menopausal age-groups had a steeper slope than men.

With increased age, many changes occur in humans, such as: i) The function of pancreatic islets gradually declines; ii) tissue sensitivity to insulin and insulin receptor activity slowly decrease; and iii) muscle tissue gradually reduces and the consumption of glucose generally decreases. Under the combined effect of these factors, blood glucose increases with age incrementally, so that the HbA1c levels are also elevated, especially with advancing age. Moreover, linear regression

analysis showed that HbA1c levels rose by 0.014% per decade in HbA1c <6.5% individuals, confirming three previous reports (21,25,26) that indicate age is a significant independent impact factor of HbA1c.

The strengths of our study are the large sample size, the strict but random selection of the population and the wide range of the age distribution. Although our study has an obvious limitation, that of greatly different numbers of men and women participants, we feel that our results are compelling and indicative of the need for further research.

In conclusion, the present study clearly illustrates the effect of gender and age on HbA1c values in Chinese populations, which illustrates the diagnostic titer of HbA1c for diabetes varies in different age/gender groups. Therefore, we suggest that age and gender should be considered in the application of HbA1c for the diagnosis of diabetes.

Acknowledgements

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