Original Article

Bimodal distribution of fasting plasma glucose in the Uyghur and Han populations of Xinjiang, China

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Background and Objectives: Bimodality in fasting plasma glucose (FPG) distribution has been detected in several populations. However, information regarding this phenomenon among Chinese ethnic groups is minimal. This study aimed to describe and update the distribution of FPG in the Uyghur and Han populations of Xinjiang, China, as well as to estimate the cut points of FPG on the basis of bimodal distribution. **Methods and Study Design:** A cross-sectional study was performed among the Uyghur and Han populations of Xinjiang, China in 2013. Questionnaire survey and FPG tests were conducted among 5,923 participants aged 20-80 years. We fitted the unimodal and bimodal distributions into the FPG data by ethnicity, age, gender, and location to test whether the FPG values were consistent with a bimodal distribution. **Results:** The FPG distribution could be described as bimodal, except for the age group of 50 years old and below among the Uyghur and Han populations and the age group of 70-80 years old among the Uyghur population ($p<0.01$). However, most of the cut points estimated using this method did not fall between the corresponding means of the first and second modes. **Conclusions:** Although a bimodal distribution of FPG was observed in the Uyghur and Han populations of Xinjiang, China, the cut points estimated using this method were not biologically meaningful, and thus, a bimodal distribution of FPG was not useful for defining cut points to diagnose diabetes in Xinjiang.

Key Words: bimodal distribution, fasting plasma glucose, diabetes, Uyghur population, Han population

INTRODUCTION

Diabetes mellitus is a worldwide public health issue with an increasing prevalence.[1] Numerous methods have been used to estimate the cut points for diagnosing diabetes, one of which is the bimodal distribution of glycemia.[2] The bimodal distribution of glucose has been reported in several populations, including Pima Indians,[3] Micronesian Naruans,[4] Mexican Americans,[5] and Egyptians,[6] among others. The basic idea of a bimodal distribution of glycemia can be briefly explained as follows. The distribution of glycemia in a population can be divided into two distinct entities to separate individuals into normal and diabetic. The prevalence of specific diabetic complications, such as retinopathy and nephropathy, is considerably higher in subjects falling into the uppercomponent (hyperglycemics) than those falling into the lower component (normoglycemics).[7] The cut points of fasting plasma glucose (FPG) that is defined by this method varies among different populations, e.g., 6.9 mmol/L in North America, 6.6 mmol/L in Spain, and 6.7 mmol/L in Singapore.[8] The cut point of FPG is a critical diagnostic index; hence, determining and defining the cut points ofFPG in Chinese ethnic groups is urgently required to diagnose diabetes. However, information regarding the bimodal distribution of FPG in Chinese ethnic groups is minimal.

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The Chinese population includes 56 ethnic groups. Among these groups, the Han people accounts for 93% of the total and are spread throughout the country,[9] while the number of the Uyghur population accounts for approximately 0.8% (10 million) of the total Chinese population; the Uyghur people are mostly found in Xinjiang, which is the largest provincial region in northwest China.[10] Several surveys have indicated that the distributions of FPG, i.e., the mean and standard deviation (SD) of FPG, are different between Han and Uyghur populations.[11-13] To the best of our knowledge, only one paper has investigated the bimodality distribution of FPG in China, with a small number of subjects, and no significant biomodality was found.[8] This situation strongly suggests the lack of such information in Chinese ethnic minorities.

This study aimed to 1) describe and update the distribution of FPG in the Uyghur and Han populations of Xinjiang, China; and 2) estimate the cut points of FPG on the basis of bimodal distribution.

MATERIALS AND METHODS

Samples

This study is a part of the China National Health Survey described in a previous study.[14] A multistage, stratified, cluster sampling scheme was adopted to select a representative sample of the general Uyghur and Han populations in the Xinjiang Autonomous Region from June 27 to August 3, 2013. A total of 2,863 Uyghur participants and 3060 Han participants were included in this study. The FPG of the participants were measured and they were interviewed to complete a questionnaire. The local office of the Chinese Center for Disease Control and Prevention and the government informed the participants before the study was conducted. All the participants were interviewed at the designated locations, such as village committee centers or community health service centers.

Measurements

The questionnaires were filled out by local interviewers who were fluent in both Uyghur and Handialects. Health information included age, gender, location, ethnicity, diastolic blood pressure, systolic blood pressure, as well as alcohol drinking and smoking habits. Blood pressure was measured thrice consecutively with a 1 minute interval between measurements while the participant was seated after resting for 5 minutes (Omron HEM-907). The blood pressure was obtained by averaging the three consecutive readings. Obesity was assessed via body mass index (BMI, weight in kilograms divided by the square of height in meters) by measuring weight using a bioelectrical impedance analysis system (Tanita BC-420). Weight and height were obtained to the nearest 0.1 kg and 0.1 cm, respectively. After 8 hours of overnight fasting, venous blood samples were collected from each subject and kept in a vacuum tube during the time of the interview. The samples were processed at the examination center and then shipped to a laboratory in Beijing. The samples were stored at −80 °C before analysis. FPG values were determined using an enzymatic method at the Peking Union Medical College Hospital.

Statistical analysis

Analyses were performed using R version 3.1.1. The FPG values were log-transformed before the unmoral and bimodal distributions were fitted to reduce skewness. The probability density functions for the unimodal and bimodal distributions were as follows[8]:

Unimodal model:

$$f(x,\mu,\sigma) = \frac{1}{\sigma\sqrt{2\pi,}}\exp de\frac{-(x-\mu)^2}{2\sigma^2})$$

Bimodal model:

$$f(x) = \pi f(x;\mu_1,\sigma_1) + (1-\pi)f(x;\mu_2,\sigma_2)$$

Where μ and σ are the mean value and SD of x, respectively; and π and $1-\pi$ are the mixture proportions in the bimodal model. We fitted a unimodal distribution using the maximum likelihood method as well as a bimodal distribution through the expectation–maximization (EM) algorithm (using FlexMix from the FlexMix package in R).[15] We used a likelihood test to compare the bimodal and unimodal distributions of FPG to determine whether FPG distribution was consistent with bimodal distribution.[16] The p value was calculated on the basis of a χ^2 distribution with 6 df because the variances of the two components were unequal in the bimodal distribution.[17] The cut point for diagnosing diabetes was determined from the crossing point of the bimodal model for two normal distributions, and its corresponding 95% confidence interval (CI) was estimated by bootstrapping.[18]

RESULTS

The baseline characteristics associated with the distribution of FPG in both the Uyghur and Han populations are described in Table 1. Subjects with diabetes were excluded (n=330). The Uyghur population was significantly younger than the Han population for both genders (p<0.05). No difference in BMI was noted between the male Uyghur and Han populations (p>0.05). By contrast, the female Uyghur population had a significantly higher BMI than the female Han population (p<0.05). The prevalence of drinking was 59.3% among the male Uyghur population and 80.3% among the male Han popula-

Table1. Base characteristics of the study population

	Uyghur	Han
Men		
N	965	1168
Urban (%)	50.1	64.3
Age (years)	46.2±14.4*	47.5±13.5
BMI (kg/m^2)	25.2±3.8	25.0±3.6
SBP (mm Hg)	123.1±15.8	123.8±14.8
DBP (mmHg)	73.7±11.3*	76.7±11.0
Alcohol drinking (%)	59.3*	80.3
Smoking (%)	70.8	73.6
Women		
N	1771	1689
Urban (%)	45.6	63.0
Age (years)	43.6±11.5*	47.4±12.2
BMI (kg/m^2)	25.9±4.7*	24.2±3.6
Systolic BP (mmHg)	116.7±18.1	116.4±16.9
Diastolic BP (mmHg)	72.0±11.8	71.8±10.4
Alcohol drinking (%)	0.7*	26.7
Smoking (%)	0.2*	2.0

*Denote p<0.05 for the difference between Uyghur and Han population. Subjects with diabetes were excluded.

Table 2. Results of the bimodal model by ethnicity and age

Ethnicity	Age (year)	N	First mode		Second mode		Percent in second mode	*p* value	Cut point
			μ	σ	μ	σ			
Uyghur									
	20-49	1892	—	—	—	—	—	—	—
	50-59	493	5.1	0.7	6.5	2.4	5.6	<0.01	7.0
	60-69	277	5.0	0.7	8.0	3.1	4.7	<0.01	7.2
	70-80	74	—	—	—	—	—	—	—
Han									
	20-49	1726	—	—	—	—	—	—	—
	50-59	647	5.1	0.6	6.6	2.3	4.9	<0.01	6.9
	60-69	322	5.2	0.6	6.1	1.5	2.5	<0.01	7.1
	70-80	162	5.2	0.6	7.4	3.8	3.1	<0.01	7.3

Data for means, SD and cut points are in mmol/L. Subjects with known diabetes were excluded. *p* value denotes the level of significance of the bimodal distribution over the unimodal distribution.

Table 3. Results of the bimodal model by gender, location and ethnicity

Gender/Location	Ethnicity	n	First mode		Second mode		Percent in second mode	*p* value	Cut point
			μ	σ	μ	σ			
Men									
	Uyghur	377	5.0	0.7	8.2	3.3	5.3	<0.01	7.2
	Han	491	5.1	0.6	6.5	2.5	4.9	<0.01	7.0
Women									
	Uyghur	467	5.1	0.7	6.5	2.4	4.9	<0.01	7.1
	Han	640	5.1	0.6	6.6	2.1	3.1	<0.01	7.0
Urban									
	Uyghur	233	5.3	0.7	7.8	3.9	5.6	<0.01	7.4
	Han	637	5.1	0.6	6.7	1.9	3.3	<0.01	6.8
Rural									
	Uyghur	606	4.9	0.7	7.2	2.5	4.6	<0.01	6.9
	Han	493	5.2	0.7	6.5	2.7	3.9	<0.01	7.2

Data for means, SD and cut points are in mmol/L. Subjects with known diabetes were excluded. *P* value denotes the level of significance of the bimodal distribution over the unimodal distribution.

tion. Only 0.7% of the female Uyghur population had a drinking habit, whereas the corresponding proportion among the female Han population was 26.7%.

Table 2 shows the results of the bimodal models by age among the Uyghur and Han populations, with all the participants aged 20-49 years combined in one group. The likelihood test indicated that the bimodal model fitted the FPG data was significantly better than the unimodal model in the 50-59 years and 60-69 years age groups in both the Uyghurand Han populations and in the 70-80 years age group in the Han population ($p<0.01$). Variation in the mean FPG values of the first mode was minimal among the Uyghur and Han populations, whereas the mean values of the second mode varied from 6.5 mmol/L to 8.0 mmol/L in the Uyghur population and from 6.1 mmol/L to 7.4 mmol/L in the Han population. No differences in the percentage of participants of the second mode were found for the age groups of 50-59 years and 60-69 years in the Uyghur population ($p>0.05$). Meanwhile, the percentage of the second mode also did not change significantly with increasing age in the Han population ($p>0.05$). The cut points ranged from 7.0 mmol/L (95% CI 6.1-7.5) to 7.2 mmol/L (95% CI 5.4-7.7) in the Uyghur population and from 6.9 mmol/L (95% CI 6.3-7.3) to 7.3 mmol/L (95% CI 3.5-7.4) in the Han population. The cut points were higher than the mean FPG values of the second mode except for the age group 60-69 years in the Uyghur population and the age group 70-80 years in the Han population.

For participants who were over 50 years old, bimodal distribution was also fitted by gender, location, and ethnicity. The results are presented in Table 3. The bimodal model was considerably superior to the unimodal model among the Uyghur and Han populations in both genders ($p<0.01$). The cut points were 7.2 mmol/L (95% CI 6.5–7.7) in the male Uyghur population, 7.0 mmol/L (95% CI 6.4–7.3) in the male Han population, 7.1 mmol/L (95% CI 5.4–7.7) in the female Uyghur population, and 7.0 mmol/L (95% CI 5.5–7.3) in the female Han population. The cut points of FPG were higher than the means values of the second mode except in the male Uyghur population. We repeatedly fitted the bimodal distribution by location and ethnicity. The bimodal models were also superior to the unimodal models among urban residents and rural residents ($p<0.01$). The cut points were 7.4 mmol/L (95% CI 3.6-7.8) in the urban Uyghur population, 6.8 mmol/L (95% CI 5.7-7.0) in the urban Han population, 6.9 mmol/L (95% CI 6.1-7.4) in the rural Uyghur population, and 7.2 mmol/L (95% CI 6.3-7.6) in the rural Han population. The cut points were higher than the means value of the second mode except in the urban Uyghur population and the rural Uyghur population. Figure 1 shows the histograms of the distributions of FPG concentrations among the Uyghur and Han populations in urban areas. The fitted bimodal smooth curves were superimposed.

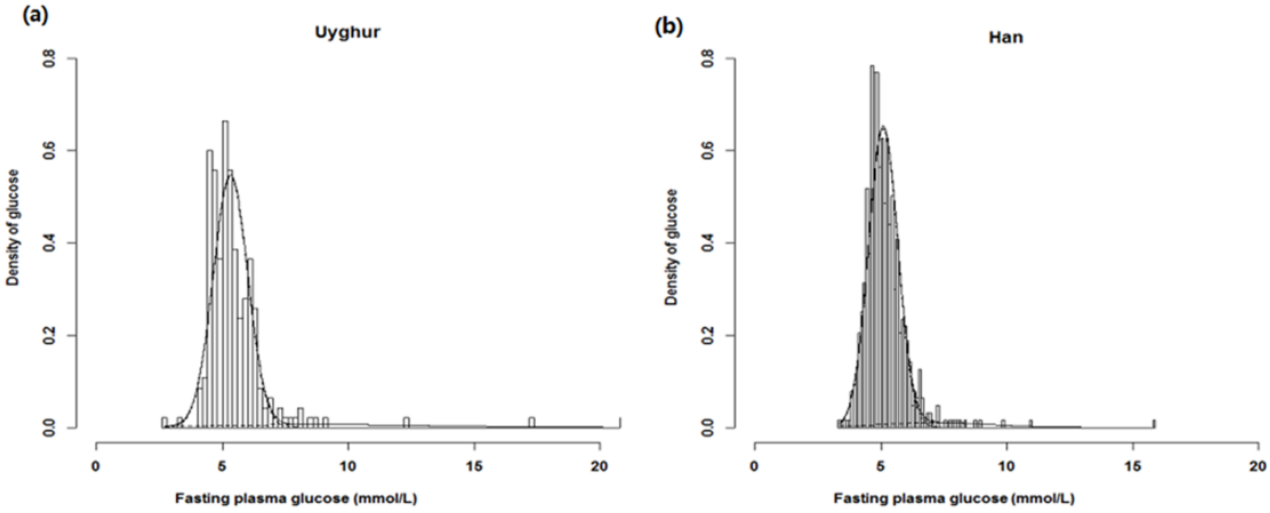

Figure 1. Distribution of FPG in Uyghur and Han population living in urban areas. (a) Distribution of FPG in Uyghur population living in urban areas. (b) Distribution of FPG in Han population living in urban areas.

DISCUSSIONS

Subjects diagnosed with diabetes may be treated through medication or lifestyle changes, which reduce the FPG value to normal. A treatment bias could be present, and thus, subjects diagnosed with diabetes were excluded in this study. Our results indicated that the distribution of FPG should be described as bimodal rather than unimodal among the participants except for the subjects below 50 years old in both the Uyghur and Han populations and those who were 70-80 years in the Uyghur population. In the bimodal distribution of FPG, the first mode represented the normal participants, whereas the second mode represented the diabetic participants.[19] The failure to produce a bimodal distribution for participants below 50 years old might be explained by the low prevalence of diabetes in this age group, which made detecting the second mode impossible. Bimodal distributions have always been reported in populations with a high prevalence of diabetes.[20,21] This finding is a potential limitation for using this method. Moreover, a bimodal model could also not be detected in the Uyghur population aged 70-80 years (n=74). A possible reason for this finding is the insufficient sample size, which leads to a lack of adequate power to detect the second mode in the bimodal model.[16]

The cut points of FPG were slightly higher in the Uyghur population than in the Han population. The different lifestyles of these groups might have caused such a discrepancy. Increased physical activity is associated with low blood glucose level.[22,23] The Uyghur ethnic group has its own unique culture and conventions that are characterized by the desire to dance and sing during spare and leisure time, which decreases the likelihood of suffering from diabetes to a certain extent. In addition, genetic factors and gene–environment interactions should also be considered.[24]

As a diagnostic criterion, the cut point of FPG based on the bimodal model should be biologically meaningful; that is, the corresponding cut point should fall between the mean values of the first and second modes in this bimodal model.[8] Our results showed that most cut points among the Uyghur and Han populations were higher than

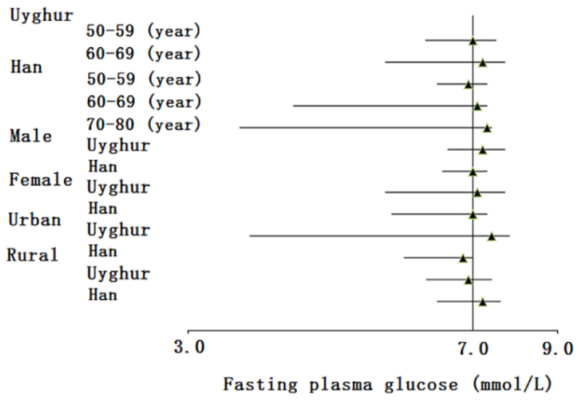

Figure 2. Cut points (95% CI) for fasting plasma glucose in Uyghur and Han population.

the mean values of the second mode. In addition, the cut points also varied between the Uyghur and Han populations. Thus, the bimodal distribution of FPG was not useful for defining the cut points to diagnose diabetes. This result is consistent with a preceding study, which showed the bimodality distribution of FPG among participants from Harbin and Qingdao where in a similar conclusion was been drawn.[8] Other rational approaches, such as the method based on the optimization program regarding the relationship between glucose level and biomarkers, should be studied further to define cut points.[25]

This study also has several limitations, such as the limited sample size in some subgroups and the lack of a bias when subjects with diagnosed diabetes were excluded. Subjects with diagnosed diabetes are known to have higher FPG before the disorder is treated with medication or lifestyle changes. If the bimodal model was present, then the patients should be under the second mode. Excluding subjects with known diabetes would effectively reduce the second mode. Adjusting the FPG value of a treated patient to its untreated level might be an effective solution for this problem. However, this technique was difficult to implement in this analysis.

In conclusion, although the bimodal distribution of

FPG was found in the Uyghur and Han populations of Xinjiang, the cut points estimated using this method were not biologically meaningful. Accordingly, the bimodal distribution of FPG was not useful for defining the cut points to diagnose diabetes in Xinjiang.

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AUTHOR DISCLOSURES

The authors declare that they have no conflicts of interest. This study was approved by the bioethical committee of the Institute of Basic Medical Sciences, the Chinese Academy of Medical Sciences (approval NO. 028-2013). This study was supported by the National Science & Technology Pillar Program during the 12th Five-year Plan Period, Grant 2012BAI37B02 from the Ministry of Science and Technology, Beijing, People's Republic of China.

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