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Age-and-sex Specific Profile of Temporal Fasting Plasma Glucose Variability in a Routine Health Screening Population

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Abstract

Background

Fasting plasma glucose (FPG) variability is an important predictor of mortality, mainly in patients with a poor glycemic control. This study aims to explore the temporal age-and-sex specific profile of temporal FPG variability in a routine health screening Chinese population and to guide the prevention and control of diabetes for targeted public health intervention.

Methods

We used the general linear model to compare differences of temporal FPG values between gender and across age groups of 101886 Nanjing residents who took part in the routine physical health examination at the Health Management Center, the First Affiliated Hospital of Nanjing Medical University in 2018. Variability of FPG caused by time, age and gender independently or in combination was analyzed.

Results

The participants included 57455(56.4%) males and 44431(43.6%) females, with the mean age of 42.8±15.0 years. The average FPG level was 5.5±1.1 mmol/L. The monthly variation contributed 22% of the overall FPG variability. A significant main effect for age group was observed ($F=7.39$, $P<0.05$), with a good fitting effect (Eta-squared =0.15). Variability of FPG showed gender differences by comparing the percentage differences of coefficient of variation which was higher in males than females. There were significant interaction effects of month*age*gender and day*age*gender.

Conclusions

Temporal variability of FPG is obvious in the general Chinese population, which is affected by both age and gender. To avoid complications associated with FPG variability such as hypoglycemia, interventions should be directed at females and males at specific ages for optimal control of FPG variability and reducing the risk of diabetes and cardiovascular outcomes.

Keywords: fasting plasma glucose; diabetes; variability; temporal; coefficient of variation

Background

Human health outcomes are unequally distributed throughout populations [1]. Due to differences among population groups subdivided according to age and other demographic characteristics over time, there is a need for epidemiological studies to evaluate observed trends, plan for health care services, and lunch interventions to improve health [2, 3].

A fasting plasma glucose (FPG) test is usually used in the diagnosis of diabetes. Plasma glucose levels are controlled by the release of insulin to ensure a dynamic equilibrium (homeostasis). Glycemic or glucose variability makes it difficult to achieve good glycemic control. Generally, blood sugar levels between 100 mg/dL (5.6 mmol/l) and 70 mg/dL (3.9 mmol/l) are considered normal. It was evident that glucose variability (GV) plays a role in the development of diabetic complications, particularly in cardiovascular events [4, 5]. FPG variability is an important predictor of mortality, mainly in patients with a poor glycemic control [6]. Elevated blood glucose has been estimated to cause 3.4 million deaths in 2004, equivalent to 5.8% of all deaths [7, 8]. Reduced glycemic exposure effect on the development and progression of microvascular complications of diabetes was reported in the Diabetes Control and Complications Trial [9] and the UK Prospective Diabetes Study [10]. Hypoglycemia has been linked to cardiovascular events and increased dementia [11, 12]. Impaired glucose tolerance and impaired fasting glycaemia are risk categories for future development of diabetes and cardiovascular disease. Generally, lowering the glucose level is essential in the treatment of diabetes, with apparent beneficial effects on microvascular and macrovascular outcomes. Nevertheless, patients with the same glycosylated hemoglobin levels and mean glucose values can have markedly different daily glucose variance [13].

Time-dependent FPG variation, as represented by coefficient of variation (CV), could predict mortality in subsequent all-cause, expanded or nonexpanded cardiovascular disease-related mortality independent of mean FPG, renal function, mean hemoglobin A1C (HbA1C), HbA1C variation, and other risk factors in patients with type 2 diabetes, suggesting that GV may be a valuable clinical biomarker in the management of patients [5, 14]. Day-to-day self-monitored FPG variability is found to be related with the risk of hypoglycemia in insulin-treated patients with diabetes [15].

For interventions to modify risk factors related to impaired glycemic control and diabetes, there is a need to identify populations at risk for developing impaired fasting glucose (IFG) and diabetes, and find measures to curb the progression. Uncontrolled and progressive increase in FPG can predict impending IFG and diabetes. In the current study, we explored the variability of FPG among a general population in eastern China in order to reveal the blood glucose distribution per age and sex for a targeted public health intervention.

Methods

Study subjects

This cross-sectional study involved 101886 Nanjing residents who took part in the physical health examination at the Health Management Center of the First Affiliated Hospital of Nanjing Medical University in 2018. FPG test was done after an overnight or at least 8 to 12 hours fast for all participants. To avoid potential source of selection bias, we included all people attending the routine health screening program in the whole year.

Definition and measurement

A fasting blood sugar level between 70 mg/dL (3.9 mmol/l) and 100 mg/dL (5.6 mmol/l) is considered normal, from 100 to 125 mg/dL (5.6 to 6.9 mmol/L) is considered prediabetes or IFG, and over 126 mg/dL (7 mmol/L) is considered diabetes [7]. IFG or prediabetes is a state of higher than normal FPG concentration, but lower than the diagnostic cut-off for diabetes. GV is defined as swings in glucose levels or deviation from steady-state (homeostasis).

Statistical modeling

General linear model (GLM) restricted to one dependent variable, univariate for a basic model for multiple linear regression is $Y_i=\beta_0+\beta_1 X_{i1}+\beta_2 X_{i2}+ \cdots +\beta_P X_{iP}+\varepsilon_i$ for each observation (i = 1, ..., n). That is n observations of one dependent variable and p independent variables. Y_i is the i^{th} observation of the dependent variable, X_{ij} is the i^{th} observation of the j^{th} independent variable, j =1, 2, ..., p. The values of β_j represent parameters to be estimated, and ε_i is the i^{th} independent identically distributed normal error. The GLM system of equations where the voxel time course, the beta values, and the residuals as vectors, and the set of predictors as a matrix using matrix notation:

$$\begin{bmatrix} y_1 \\ \vdots \\ y_n \end{bmatrix} = \begin{bmatrix} 1 & X_{11} \dots & \dots X_p \\ \vdots & \vdots & \vdots \\ 1 & X_{n1} \dots & \dots X_{np} \end{bmatrix} \begin{bmatrix} b_0 \\ \vdots \\ b_p \end{bmatrix} + \begin{bmatrix} e_i \\ \vdots \\ e_n \end{bmatrix} \Longrightarrow y = Xb + e$$

Time courses of the signal, predictors, and residuals have been arranged in column form with time running from top to bottom as in the system of equations. The matrix X represents the design matrix containing the predictor time courses as column vectors. The beta values now appear in a separate vector b. The term Xb indicates matrix-vector multiplication.

GLM diagnostics

A good fit would be attained with beta values, b leading to predicted values $\hat{y}$, which are as close as possible to the measured value y, implying small errors:

$\hat{y} = Xb,\ e = y - \hat{y},\ e'e = (y - Xb)'(y - Xb) \rightarrow \min$ finds optimal beta weights minimizing the squared error values (the "least squares estimates"), $b=(X'X)^{-1}X'y$, where X'X matrix, corresponds to the predictor variance-covariance matrix and X'y, the scalar product which evaluates to a vector containing as many elements as predictors. Also, the variance of the measured time course can be decomposed into the sum of the variance of the predicted values (model-related variance) and the variance of the residuals: var(y)=var(yˆ)+var(e). The square of the multiple correlation coefficient, R^2=var(yˆ)/var(y), provides a measure of the proportion of the variance of the data, which can be explained by the model. The larger, the better.

GLM assumptions and significance tests

The population error values ε must have an expected value of zero at each time point, i.e. $E[\varepsilon_i] = 0$, and constant variance, i.e. $Var[\varepsilon_i] = \sigma^2$. The error values are assumed to be uncorrelated, i.e. $Cov(\varepsilon_i, \varepsilon_j) = 0$ for all i = j, assumed to be normally distributed ($e_i \sim N(0, \sigma^2)$, normal i.i.d) to justify the use of t and F distributions in hypothesis tests. The multiple correlation coefficient is an important measure of the "goodness of fit" of a GLM. The R value can be transformed in an F statistic with p - 1 degrees of freedom in the numerator and n - p degrees of freedom in the denominator: $F_{n-1,n-p}=R^2(n-p)/(1-R^2)(p-1)$ in order to test whether a specified model significantly explains variance in a voxel time course. Comparisons between conditions can be formulated as contrasts, which are linear combinations of beta values corresponding to null hypotheses, $H_0: b_i = 0$. A t value for a specific contrast can be converted in an error probability value *P* using the equation, $t = c'b/\sqrt{var(e)c'(X'X)^{-1}c}$,

where H_o: c'b = 0 and H_a: c'b = 0. If this *P* value is smaller than 0.05 and positive, the alternative hypothesis may be concluded.

The GLM univariate procedure provided regression analysis and analysis of variance for FPG and FPG categories (<5.6 mmol/L, 5.6-6.9 mmol/L, and >=7.0 mmol/L). We tested the null hypotheses about the effects of various age groups and different gender on the means of the FPG category and investigated interactions between temporal factors and individual effects. A Tukey test was applied for post-hoc analysis if an overall F test statistical significance was observed to evaluate differences among specific means. Estimated marginal means gave estimates of predicted mean values for the cells in the model, and profile plots were used to visualize the interaction of these means.

Data were given as mean together with standard deviation (SD), and cross-tabulation of FPG were estimated by age, sex, height, weight, SBP, DBP, and BMI. Observed trends of FPG over days, months, and seasons were explored for inter-individual variability with respect to age and sex. All analyses were performed with SPSS 25 and *P* value < 0.05 was considered statistically significant.

Measures of variability

The measures of variability, such as variance, SD, and coefficient of variation, have different strengths and applications. Though SD is generally preferred over variance because of its easy interpretation, the coefficient of variation has its power when it comes to compare data from different populations [13] (Supplementary Table S1).

Ethical statement

This study was approved by the ethics committee of Nanjing Medical University. Data used in this study were anonymized and irreversibly de-identified to protect participants, health care professionals, and hospital privacy.

Results

The participants included 57455 (56.4%) males and 44431 (43.6%) females. Their mean age was 42.8±15 years (range 12-100 years). The overall FPG was 5.59±1.1 mmol/L with the inter-quartile of 5.0-5.7 mmol/L. The overall CV of FPG was 0.2, which implied SD was 20% of its mean value (Table 1).

The monthly FPG variation revealed the mean value of 5.4±1.07 mmol/L (range 4.3-26.3 mmol/L), with inter-quartile range of 5.0-5.7 mmol/L. The seasonal FPG variation also showed the mean value of 5.2±1.23 mmol/L (range 4.3-6.7), with the inter-quartile range of 4.8-5.5 mmol/L. In all, the monthly variation contributed 22% of the overall FPG variability (Figure 1).

FPG values for males and females were 5.7±1.3 mmol/L and 5.3±0.9 mmol/L, respectively. A one-way ANOVA revealed that there was a significant FPG difference between nine age groups ($F(8, 94145) = 1571.5$, $P < 0.001$). A Tukey honest significant difference (HSD) test revealed that all nine means were significantly different from each other though there was a slight deviation from this pattern for males in 70-79 years and a sharp deviation for those older than 90 years in both sexes. The gender*gender mixed model revealed that the main effect of gender was significant ($F(1, 94154) = 83.461$, $P < 0.05$). Thus, there was an overall significant difference of FPG means between males and females. A significant main effect

for age group was obtained (F (8, 94154) =7.39, P <0.05), with a good fitting effect (Eta-squared =0.15). FPG variability was higher in males than that in females. Variability of FPG showed gender differences by comparison of CV percentage differences and PDs:PD =100(CV_{male} - CV_{female})/CV_{female} showed gender differences (gender variability ratio =35.3% more in males than females) (Table 2).

We observed significant interactions of month*age*gender (F(82, 94072) =1.89, P <0.001) and day*age*gender (F (35, 94119) =1.45, P <0.05). However, there were no significant interaction effects of season*age*gender (F (23, 94131) =1.50, P = 0.10) and half-year*age*gender (F(8, 94146) =1.41, P =0.19), respectively. Thus, the month and day significantly attributed to the variability in FPG whereas season and half-year did not.

The amplitude percent mean, $(\mathrm{A\%M} = (\text{highest FPG} - \text{lowest FPG})/(\text{mean FPG}) * 100)$, for males and females were 24.7% and 24.5%, respectively. The SD percent mean, $(\mathrm{SD\%M} = (\text{SD of FPG values})/(\text{mean FPG}) * 100)$, was higher in males (22.8%) than that in females (17.0%). Examination of the multiple comparisons by age group and month were significant from January to December except for September (MD =0.014, 95% CI: -0.02-0.04, P =0.37). The highest and lowest FPG values were recorded in August on Wednesday and March on Thursday in males, respectively. Among the females, the highest and lowest FPG values were recorded in January on Wednesday and June on Sunday. Those aged 80-89 years in both sexes recorded the highest FPG mean values while the lowest was among 10-19 years for males and 20-29 years for females (Figure 2).

The age was associated with an increased IFG for both sexes where those in 50-59 years recorded the highest proportion (23%). Women aged 30-39 years and men aged 40-49 years had an increased risk of type 2 diabetes (Table 3).

Discussion

In this study, we observed a significant variability of FPG caused by month, age, or gender. Mean glucose is an indicator that high or low blood sugars are common for hyperglycemia or hypoglycemia occurrence in order to determine the best action, such as differently timed exercise or a lower medication dose, however the variation of blood sugar level should not be neglected. Though it is ideal to have the lowest possible average glucose, from the Diabetes Control and Complications Trial (DCCT) and United Kingdom Prospective Diabetes Study (UKPDS), it should be without frequent, prolonged, or severe hypoglycemia.

A follow-up of blood glucose distribution characteristics in a health examination population in Chengdu, China, from 2010 to 2016 showed higher levels of glucose with ages increasing, and males indicated higher expression of glucose than that in females [16]. Likewise, the mean level of FPG significantly increased across age groups in both males and females. The mean level of FPG was higher in males compared to that in females. It was evident that in the Kailuan cohort, both males and females showed higher percentage of diabetes with ages increasing, and males showed higher percentage of diabetes compared with females in the same age group. Our findings were not different from that, by which the normal level of glucose was higher in aged population as compared with the young participants, and the percentage of males with IFG or at risk of type 2 diabetes was higher than that of females [6]. Our results add evidence that high variability in FPG may be associated with adverse health outcomes among different age groups in a ‘healthy’ population.

The Taichung Diabetes Study measured glycemic variability by computing annual CV of all FPG measurements within each year, and showed that annual CV of FPG was independently associated with all-cause mortality in patients with type 2 diabetes aged 30 years and over [17]. The Verona Diabetes Study found that FPG variability, as assessed by CV of FPG over a period of three years, was an independent predictor of all-causes in patients with type 2 diabetes aged 56–74 years [18]. From our study, FPG variability showed gender differences by comparison of CV percentage differences, PDs/PD=100(CVmale - CVfemale)/CVfemale) showed gender differences (gender variability ratio=35.3% more in males than females) where month and day were attributable to FPG variability.

A better understanding of these differences among the population is critical for implementing effective preventive measures. Participants classified based on FPG category revealed that the risk of IFG and diabetes were associated with maximal swings of high SD and CV. The most straightforward and easy way to measure inter-day variability is calculating the SD of fasting blood glucose concentrations [19]. Siegelaar suggested SD as the easiest, best validated measure and preferable method when quantifying variability from CGM data [13]. Low SD reflected a steady glucose level with minimal swings. CV normalized glucose variability for different mean glucose levels. The larger the variability, the greater the risk of hypoglycemia.

Population density is relatively high in eastern China and knowing its demographic transition within and across age groups and gender is a major key for a public health intervention to improve overall health. To control FPG and avoid complications associated with FPG variability such as hypoglycemia, there is the need for treatment

strategies to control fluctuations in FPG variability in order to reduce the risk of diabetes and cardiovascular outcomes.

This study has several limitations. First, the variability of FPG may be underestimated due to the short length of study. Second, this was an age-and-sex specific profile of FPG over time, but there could be other factors that might be attributed to the FPG variability. Third, models other than GLM could be used for further studies. Thus, generalizability of the study results should be cautious by considering the characteristics of different populaitons.

Conclusion

Temporal variability of FPG is obvious in the general Chinese population, which is affected by both age and gender. Interventions should be directed at females and males in the 30-39 years and 40-49 years respectively for optimal control of FPG variability. Also, people should be encouraged to do self-monitoring fasting blood glucose checks and report unusual changes in blood sugar patterns for early treatment to avoid risk of diabetes and cardiovascular diseases.

List of abbreviations

ADA: American Diabetes Association; CV: Coefficient of Variation; FPG: Fasting Plasma Glucose; GLM: General Linear Model; GV: Glucose Variability; IFG: Impaired Fasting Glucose; MD: Mean Difference; SD: Standard Deviation

Declarations

Ethics approval and consent to participate: This study was approved by the ethics committee of Nanjing Medical University. Written informed consent was obtained from study participants. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication: Not applicable

Availability of data and materials: All data generated or analyzed during this study are included in this published article.

Competing interests: The authors declare that they have no competing interests

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Authors' contributions: Conceptualization, AL, XL, and JW; methodology, AL; software, AL; validation, XL, QZ and ZL; formal analysis, AL; investigation, XL and QZ; resources, XL and QZ; data curation, XL, QZ, and ZL; writing—original draft preparation, AL; writing—review and editing, AL, XL, ZL, QZ and JW; visualization, AL and JW; supervision, QZ and JW; project administration, QZ and JW; funding acquisition, JW. All authors have agreed on the journal to which the article has been submitted and agreed to be accountable for all aspects of the work.

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Figure legends

Figure 1. Temporal variability of fasting plasma glucose in a Chinese population

Figure 2. Multiple plots of temporal fasting plasma glucose variability by age and sex

A and B showing monthly distribution of estimated marginal means of FPG by age and sex

C and D showing half-year distribution of estimated marginal means of FPG by age and sex

E and F showing daily distribution of estimated marginal means of FPG by age and sex

G and H showing seasonal distribution of estimated marginal means of FPG by age and sex

FPG: fasting plasma glucose

Table 1. Overall variability assessment of participants' characteristics

Variable	mean±SD	Range	Q1	Q2	Q3	CV
Age (years)	42.8±15.0	12-100	31	40	53	0.35
Weight (Kg)	66.8±12.6	31-175	57	66	75	0.19
Height (cm)	166.7±8.2	106-202	161	167	173	0.05
BMI (Kg/m^2)	23.9±3.8	12.6-59.2	21.5	23.7	26.0	0.16
DBP (mmHg)	75.8±11.2	32-142	68	75	83	1.15
SBP (mmHg)	124.4±17.6	63-263	112	123	135	0.14
FPG (mmol/L)	5.5±1.1	1.1-26.3	5.0	5.3	5.7	0.20

Q1: lower quartile part; Q2: median; Q3: upper quartile part; CV: coefficient of variation

400 Table 2. Descriptive characteristics of participants

Variables	Age (years)									
	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	>=90	Total
Male	n=1134	n=9828	n=15119	n=12187	n=10268	n=5015	n=2555	n=1274	n=75	n=57455
Age (years)	17.9±0.7	26.0±2.4	34.4±2.9	44.5±2.9	54.0±2.6	63.9±2.8	74.3±2.9	83.3±2.6	91.8±2.1	43.8±15.2
Weight (kg)	70.3±10.7	73.7±12.2	75.6±11.1	74.5±9.8	73.5±9.3	72.0±9.4	69.2±9.3	65.9±9.8	62.1±10.3	73.7±10.7
Height (cm)	176.0±4.9	174.2±5.8	173.0±5.8	171.2±5.5	170.2±5.6	169.1±5.8	166.6±5.4	164.7±5.9	162.5±5.3	171.6±6.1
BMI (Kg/m^2)	22.7±3.3	24.3±3.6	25.2±3.3	25.4±2.8	25.3±2.7	25.2±2.8	24.9±3.0	24.3±3.2	23.5±3.4	25.0±3.2
DBP (mmHg)	67.7±6.8	74.4±9.3	77.2±10.4	81.1±11.1	82.9±10.9	81.5±10.4	78.5±10.8	75.4±11.0	70.5±11.0	78.8±11.0
SBP (mmHg)	122.7±10.1	123.9±12.6	123.8±13.8	127.2±15.8	131.5±16.9	136.6±17.9	144.6±18.6	148.1±18.7	149.4±18.3	128.4±16.5
FPG (mmol/L)	5.1±0.4	5.2±0.6	5.4±0.8	5.7±1.2	5.7±1.2	6.0±1.6	6.3±1.6	6.5±1.7	6.2±1.5	5.7±1.3
Female	n=285	n=10126	n=13574	n=8714	n=5933	n=3431	n=1561	n=771	n=36	n=44431
Age (years)	17.8±0.9	25.9±2.3	34.2±2.8	44.5±2.9	53.8±2.6	63.8±2.7	74.2±2.8	83.1±2.5	91.8±2.3	41.4±14.6
Weight (cm)	70.3±10.7	73.7±12.2	75.6±11.1	74.5±9.8	73.5±9.3	72.0±9.4	69.2±9.3	65.9±9.8	62.1±10.3	57.4±8.0
Height (Kg)	164.4±4.9	161.7±5.2	161.2±5.2	159.7±5.1	159.0±5.2	157.4±5.5	154.5±5.2	152.0±5.8	148.9±8.0	160.0±5.6
BMI (Kg/m^2)	20.6±2.7	21.1±2.7	21.9±2.8	22.9±2.9	23.4±2.9	24.2±3.3	24.4±3.3	24.2±3.5	23.7±3.4	22.4±3.0
DBP (mmHg)	67.5±7.2	69.9±8.4	69.9±9.2	72.3±10.8	75.4±10.8	76.4±10.6	74.7±10.6	73.5±11.4	72.8±11.6	71.8±10.1
SBP (mmHg)	114.7±11.2	112.5±11.4	112.2±12.7	118.0±15.7	125.9±17.5	135.0±18.3	144.5±18.3	150.3±20.3	155.1±22.5	118.9±17.3
FPG (mmol/L)	5.1±0.6	5.0±0.5	5.2±0.6	5.3±0.8	5.5±1.0	5.9±1.3	6.2±1.4	6.3±1.6	5.8±0.7	5.3±0.9

401

402 Table 3. Cross tabulation of age group by FPG category, sex, BMI and smoking status

Variable	Category	Age (years)								
		10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	>=90
Female	**FPG category**									
	<5.6	236(0.7)	7956(25.1)	10983(34.7)	6434(20.3)	3644(11.5)	1632(5.2)	561(1.8)	229(0.7)	12(0.0)
	5.6-6.9	22(0.3)	633(8.4)	1561(20.8)	1491(19.8)	1582(21.0)	1260(16.8)	633(8.4)	323(4.3)	14(0.2)
	>=7.0	1(0.1)	20(1.7)	66(5.6)	133(11.2)	244(20.5)	318(26.7)	256(21.5)	149(12.5)	2(0.2)
Male	**FPG category**									
	<5.6	988(2.9)	7521(22.0)	11041(32.3)	7150(20.9)	4694(13.7)	1753(5.1)	702(2.1)	341(1.0)	17(0.0)
	5.6-6.9	114(0.7)	1195(7.6)	3176(20.3)	3767(24.0)	3740(23.9)	2019(12.9)	1099(7.0)	531(3.4)	23(0.1)
	>=7.0	0(0.0)	49(1.3)	239(6.1)	722(18.6)	1235(31.8)	855(22.0)	551(14.2)	229(5.9)	8(0.2)
Both	**BMI**									
	<25	1126(1.6)	15944(23.0)	20137(29.0)	13455(19.4)	9866(14.2)	5003(7.2)	2456(3.5)	1335(1.9)	81(0.1)
	25-29	273(1.0)	3315(11.7)	7309(25.7)	6609(23.3)	5713(20.1)	3051(10.7)	1477(5.2)	621(2.2)	28(0.1)
	>=30	20(0.5)	695(17.0)	1247(30.5)	837(20.5)	622(15.2)	392(9.6)	183(4.5)	89(2.2)	2(0.0)
	Smoking									
	Never	1386(1.9)	15310(21.4)	20770(29.1)	13382(18.7)	9799(13.7)	5799(8.1)	3162(4.4)	1681(2.4)	88(0.1)
	Quitting	1(0.1)	87(5.6)	215(13.7)	352(22.5)	459(29.3)	290(18.5)	125(8.0)	31(2.0)	4(0.3)
	Yes	7(0.1)	1137(9.2)	2778(22.4)	3502(28.2)	3411(27.5)	1202(9.7)	317(2.6)	63(0.5)	1(0.0)

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Figures

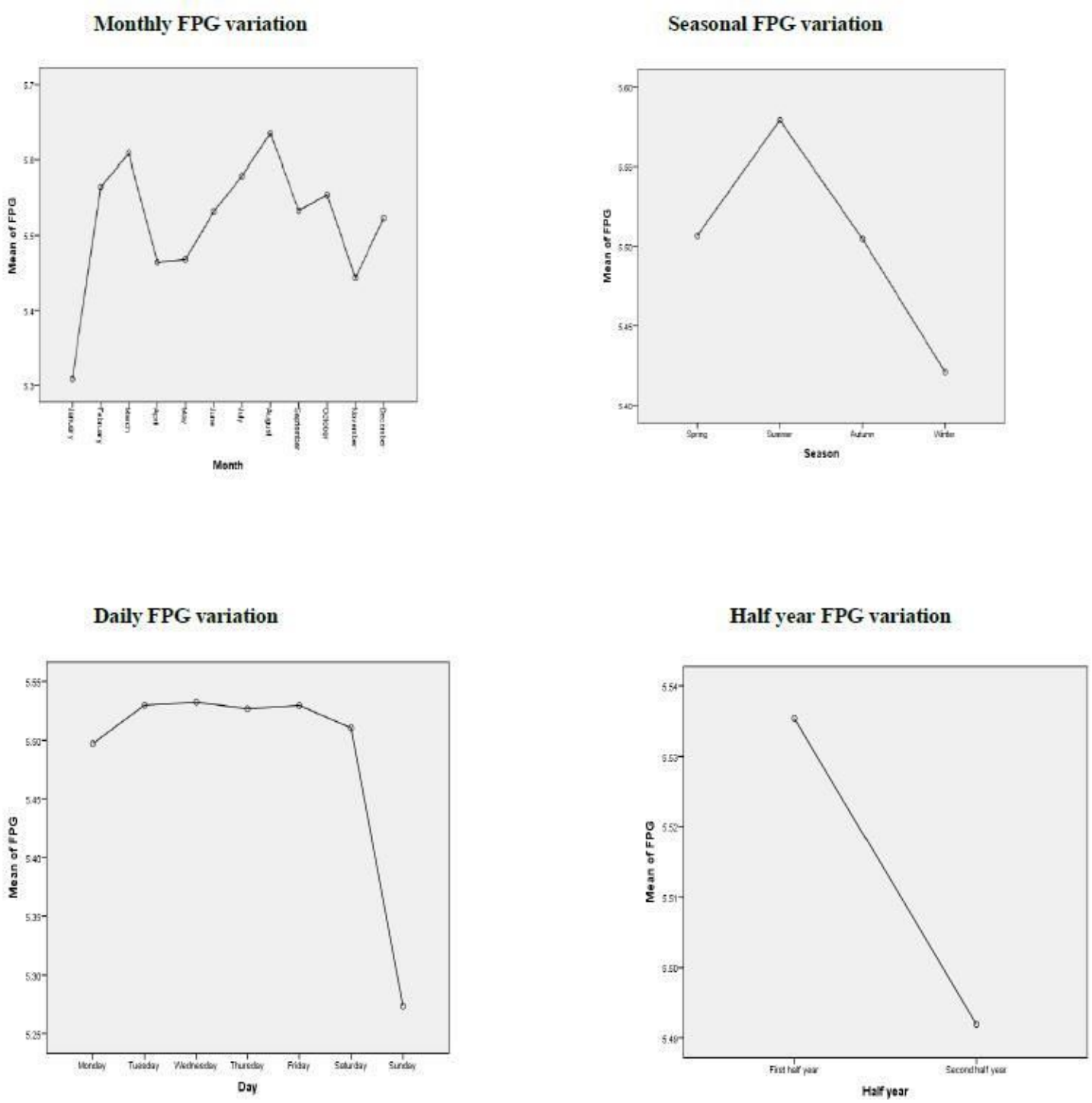


Figure 1

Temporal variability of fasting plasma glucose in a Chinese population

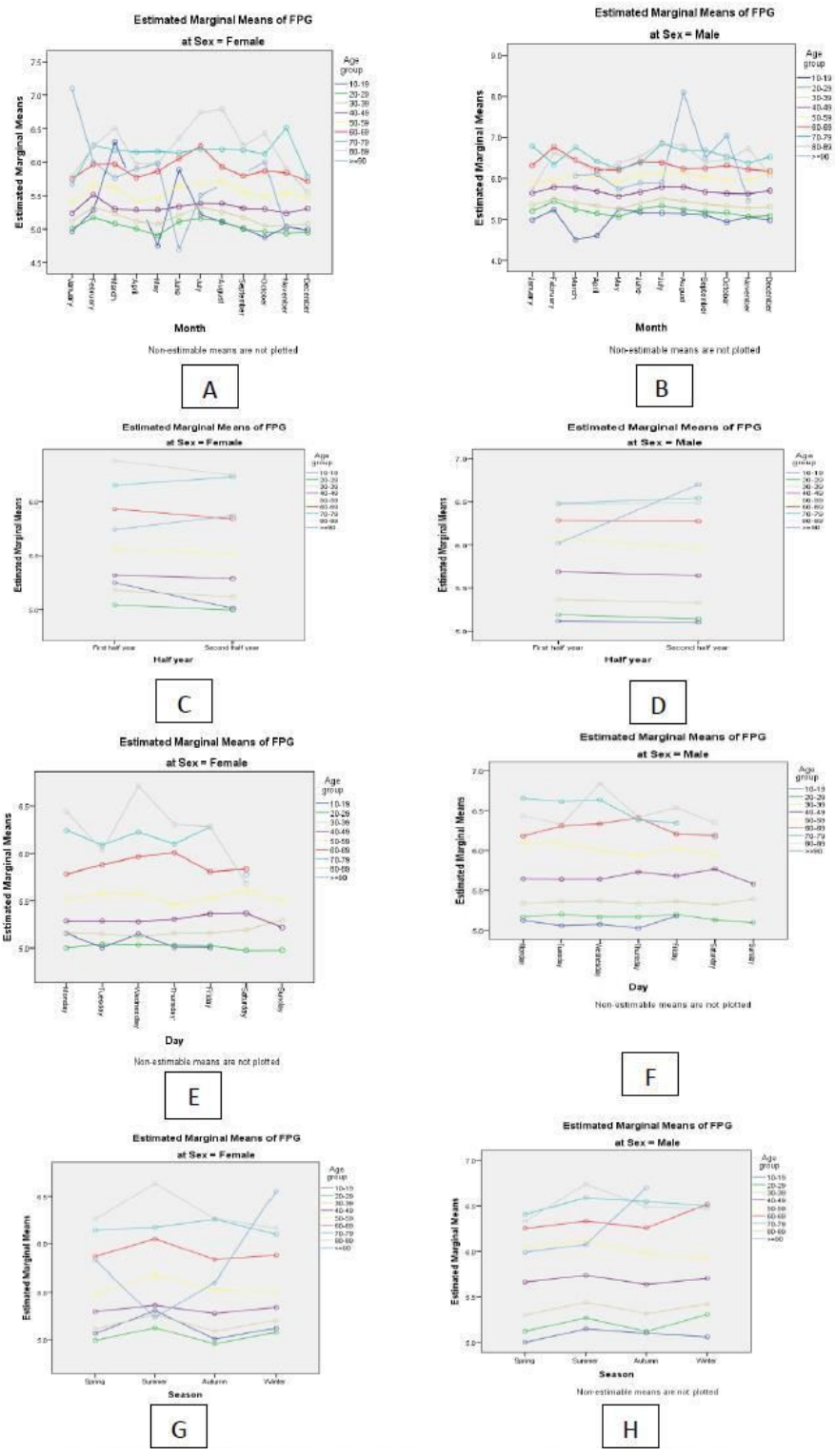


Figure 2

Multiple plots of temporal fasting plasma glucose variability by age and sex A and B showing monthly distribution of estimated marginal means of FPG by age and sex C and D showing half-year distribution of estimated marginal means of FPG by age and sex E and F showing daily distribution of estimated marginal means of FPG by age and sex G and H showing seasonal distribution of estimated marginal means of FPG by age and sex FPG: fasting plasma glucose

Supplementary Files

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- Supplementaryfiles.doc