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The patterns of glucose tolerance and insulin resistance among rural Chinese twin children, Adolescents and young adults

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Abstract

Pubertal insulin resistance (IR) is well recognized but little data is available for glucose and insulin pattern from a large, unselected lean population. This report describes the age- and gender-specific distributions of glucose tolerance and IR in a rural Chinese twin population. This report includes 4,488 subjects aged 6 to 24 years. The primary variables of interest are fasting plasma glucose (FPG), 2h post-load plasma glucose (2h PG), fasting serum insulin (FSI), 2h post-load insulin (2h PI) and the homeostatic model assessment for IR (HOMA-IR) index. Age- and gender-specific patterns for the primary variables are described using smoothing plot, arithmetic or geometric mean, and percentiles. There is an increase in FPG, 2h PG and IR during puberty (10–19 years) and return to pre-puberty level by the age of 20 years. IR peaks around age of 14 years in girls, and 16 years in boys. 2h PG and 2h PI are higher in girls than in boys from early puberty, and the gender differences are more pronounced afterward. Moreover, the prevalence of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) increase after puberty, and higher in girls than in boys. In this community based, non-obese rural Chinese twin population, we observed gender-specific remarkable pubertal surge of IR and modest increase in plasma glucose as well as increasing prevalence of IFG and IGT with age. Notably, females had higher 2h PG and higher prevalence of IFG and IGT. Our study underscored that adolescence (even more so in females) is a critical period for developing IR and pre-diabetes.

Keywords

adolescents; glucose tolerance; insulin resistance; Chinese

1. Introduction

In the last decades, the prevalence of type 2 diabetes mellitus (T2DM) has been increasing not only in adults [1], but also in children and adolescents [2–4]. By 1994, T2DM in children represented up to 16% of new cases of diabetes in urban areas [2]. In addition, a study reported the T2DM in Thai children and adolescents increased from 5% during 1986–

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Institutional approval

The study protocol was approved by the Institutional Review Boards of Children's memorial Hospital and the Biomedical Institute, Anhui Medical University in Hefei, China. All participants gave written consent.

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1995 to 17.9% during 1996–1999[3]. Numerous studies demonstrated that, similar to adults, T2DM in youth is usually accompanied by obesity, dyslipidemia, hypertension and sub-clinical immune activation [5,6]. The combination of these risk factors makes pediatric T2DM an emerging public health problem. It is generally recognized that the etiology of T2DM in adults is the combination of insulin resistance (IR) and impaired β -cell function. Moreover, studies in adults have shown that T2DM develops over a long period of time and most patients have impaired glucose regulation, an intermediate stage (pre-diabetes), before overt diabetes. Peripheral IR is the prominent finding in this stage.

It is well observed that in children and adolescents, insulin sensitivity falls when entering puberty. However, there are several important gaps in research on childhood IR and glucose tolerance. First of all, all children appear to become more insulin resistant at the time of puberty, which is associated with a number of metabolic, hormonal, and body composition changes that can influence insulin action. However, IR patterns during puberty are not well established in population-based samples. Most of the available epidemiologic information on pre-diabetes or T2DM in children and adolescents comes from case series or hospital studies, whereas population-based studies are rare.

Second, the criteria for diagnosis of diabetes and pre-diabetes in children, based on standard values of fasting plasma glucose, random plasma glucose and the oral glucose tolerance test (OGTT), are currently the same as in adults [7]. But compared with epidemiological data on pre-diabetes and T2DM in adults, data on the prevalence of T2DM or pre-diabetes in children and adolescents are rather limited. To date prevalence data exist mainly for the United States, the impact of ethnicity is also evident in studies in native American population [4,8]. The pathogenesis of pre-diabetes or T2DM in children and adolescents are not yet fully understood. The etiology of T2DM in youth is assumed to be similar as in adults in so far as it is multifactorial including genetic and environmental factors, resulting from the combination of IR and impaired β -cell function. But, the time course, degree and gender difference of IR and its contributions to pre-diabetes or T2DM as children progress through puberty remains to be determined. Therefore, further information on glucose tolerance and IR patterns and related risk factors among different ethnic groups and among people in different regions not only will facilitate population-targeted prevention, early detection and treatment of IR and T2DM, but also may provide new insight into the etiology of T2DM.

The ongoing study of metabolic syndrome in Anqing, China offered the unique opportunity to address the above mentioned gaps. Spanning 80 km along the north bank of the Yangtze River, the area of Anqing has three urban areas and eight rural counties covering 15,000 km². The rural environment, abundance of physical activity, and the high fiber and high carbohydrate content of the diet forms contrast sharply with the typical findings in urban settings in the United States. In additions, rural residents constitute a large segment of the world's total population, particularly in developing countries. In China, 85% of the population lives in rural, agricultural regions. The large family size and stable resident population permit the investigation of genetic and environmental risk factors of T2DM.

Using the data from the ongoing study in Anqing, this study describes the gender- and age-specific patterns and distributions of glucose tolerance and IR during the ages of 6–24 years. It also examines the timing of peak IR and investigates the prevalence of pre-diabetes in rural Chinese population from childhood to young adulthood. To our knowledge, this is the first study investigating these phenomena in a large, community-based, predominantly rural, relatively lean Chinese children, adolescents, and young adults.

2. Patients and methods

2.1 Study population and Procedures

This report includes data from an ongoing study of metabolic syndrome in a large Chinese twin cohort. The population-based cohort of twin pairs enrolled in Anqing, China from 1998 to 2000. Twins were identified through a multistage process. First, investigators from Anhui Medical University and the Anqing Hospital/Research Institutes held a three-day workshop in each township to train local doctors to participate in subject recruitment. The first day was used to explain the purposes, scopes, and procedures of the study. The definition of a twin was introduced and several examples were presented. Local doctors were requested to go back to their own villages to prepare a list of all twins in their practice area. Epidemiologists from Anhui Medical University checked all twin lists with the township/village doctors. Twins were chosen based on the following criteria: (1) older than 6 years, (2) both twins available, and (3) both twins (or parents/guardians of children) agreed and consented to participate in the survey. Eligible twins were invited to a central office to complete a questionnaire interview, physical examination, and oral glucose tolerance test (OGTT). Participants were required to fast at least 10 hours before the blood samples were taken. A standard OGTT (1.75g/kg or a maximum of 75 g of glucose) was performed for all subjects. Blood samples were obtained from 0 and 120 minutes after glucose administration, for glucose and insulin measurements. The study protocol was approved by the Institutional Review Boards of Children's memorial Hospital and the Biomedical Institute, Anhui Medical University in Hefei, China. All participants gave written consent.

This study focused on subjects who were 6–24 years of age. Of a total of 4,496, 0.18% (eight individuals) had fasting plasma glucose (FPG) ≥ 7.0 mmol/L and/or 2h post-load glucose (2h PG) ≥ 11.1 mmol/L and were excluded from the final analysis. 4,488 were included in this report. Of 4,488, 155 children have missing data for 2h PG and 2h post-load insulin (2h PI) measurements.

2.2 Laboratory methods

Plasma was separated from blood cell in the field within 30 min after the blood was drawn and kept refrigerated. Plasma glucose was measured within 2 hours by a modified hexokinase enzymatic method (Hitachi 7020 Automatic Analyzer, Japan). Standard quality control procedures were performed each day with standard samples that came with the reagents (CV<8%). Serum insulin was measured by electrochemiluminescence method on an Elecsys 2010 system (Roche, Switzerland). Duplicate analyses were also conducted daily using samples collected from study participants (CV<10%, mean=3%). Insulin resistance was estimated using the homeostatic model assessment for insulin resistance (HOMA-IR) index which was calculated as fasting insulin concentration (μ U/mL) $\times$ fasting glucose concentration (mmol/L)/22.5[9]. The insulin sensitivity was estimated using the quantitative insulin sensitivity check index (QUICKI) which was calculated as $1/[\log \text{fasting insulin concentration } (\mu\text{U/mL}) + \log \text{fasting glucose concentration } (\text{mg/dl})][10]$.

2.3 The definition for prediabetes

The definition for isolated impaired fasting glucose (IFG), isolated impaired glucose tolerance (IGT) and combined IFG plus IGT (IFG/IGT) was described previously [11]. Isolated IFG is defined as FPG between 5.6–6.9 mmol/L with 2h PG in OGTT of < 7.8 mmol/L, and isolated IGT as 2h PG in OGTT of 7.8–11.0 mmol/L with FPG < 5.6 mmol/L. IFG/IGT is defined as FPG between 5.6–6.9 mmol/L with 2h value in OGTT of 7.8–11.0 mmol/L.

2.4 Statistical analyses

All analyses were conducted separately by gender using SAS version 9.1 (SAS Institute, Cary, NC). This twin cohort was analyzed as individuals. First, the distributions of age- and gender- specific FPG, 2h PG, fasting serum insulin (FSI), 2h PI and HOMA-IR were examined using arithmetic mean and standard deviation (SD) for glucose measures, geometric mean for insulin and HOMA-IR, and median and percentiles for all the measurements. We calculated 95% confidence interval (CI) for means. Also, we categorized study individuals into four pubertal subgroups based on age: pre-puberty (age <10years), early puberty (10–14 years), late puberty (15–19 years) and young adult (20–24years), and presented descriptive data for each pubertal group in male and female as well. Comparisons of data among groups were tested by using gender-specific linear regressions. Generalized estimating equations (GEE) were applied to all regression models to adjust for intra-twin pair correlation, with an independent working correlation structure using the SAS GENMOD procedure. Furthermore, the patterns for glucose tolerance and IR measures are described using smoothing plots of FPG, 2h PG, log (FSI), log (2h PI), log (HOMA-IR) and QUICK levels by age in both genders. All smoothing plots used locally weighted non-parametric regression (LOESS) method with SAS procedure LOESS.

3. Results

3.1 Fasting and 2h blood glucose

Table 1 and 2 depict gender-specific means (95% confidence intervals for means), SDs, 10th percentiles, medians, and 75th, 90th and 95th percentiles for FPG and 2h PG in four puberty groups. Relative to those at pre-puberty, the mean FPG increased at early puberty (β , 95% CI: 0.1, 0.1–0.2, $p=0.0001$ in males; 0.2, 0.1–0.3, $p<0.0001$ in females) and was even higher at late puberty in both sexes (β , 95% CI: 0.3, 0.2–0.4, $p<0.0001$ in males; 0.5, 0.3–0.6, $p<0.0001$ in females). The FPG difference between late puberty and young adult was significant in females (0.3, 95%CI 0.1–0.4, $p<0.0001$), but not in males (0.08, –0.08 to 0.24, $p=0.337$). Supplementary Table 1 and 2 in the online appendix provide detailed each year age- and gender-specific means (95% confidence intervals for means), SDs, 10th percentiles, medians, and 75th, 90th and 95th percentiles for FPG and 2h PG separately. Of note, the 95th percentile values for FPG were greater than 5.6mmol/L, the cut point for IFG [12], at age 13–21 years in boys and at age 14–24 years in girls. The 2h PG 95th percentile values were more than 7.8mmol/L, the cut point for IGT [12], only at age 21–22 years in boys and 18–21years in girls.

3.2 Fasting and 2h Insulin

Table 3 delineates gender- specific Geometric means (95% confidence intervals for means), 10th percentiles, medians, and 75th, 90th and 95th percentiles for FSI in four puberty groups. The mean of log(FSI) increased about 0.2 from pre-puberty to early puberty [β (SE): 0.16 (0.05), $p=0.0007$ in males; 0.19 (0.05), $p=0.0001$ in females], peaked at late puberty [β (SE), male: 0.39 (0.07), $P<0.0001$; female: 0.20 (0.06), $p=0.0016$] and returned, at young adult, to a level that was similar to pre-puberty level [male: 0.03 (0.08), $p=0.7225$; female: –0.01 (0.05), $p=0.889$]. The pattern of 2-h PI across age (middle panels in Figure 1) was essentially similar to that of FSI. Supplementary Table 3 in the online appendix delineates each year age- and gender- specific Geometric means (95% confidence intervals for means), 10th percentiles, medians, and 75th, 90th and 95th percentiles for FSI.

3.3 Insulin Resistance

Table 4 shows the gender-specific HOMA-IR distributions in four puberty groups. The pattern of log (HOMA-IR) across age was very similar to that for log (FSI) in both genders

(Figure 1). Until the age of 10 years, log (HOMA-IR) distributions were similar in boys and girls. Geometric mean of HOMA-IR for girls briefly surpassed those for boys during age 11–14 years (Table 4, Figure 1). Interestingly, HOMA-IR 95th percentile values for girls surpassed those for boys between 15–19 years of age. At young adults, HOMA-IR pattern in boys and girls became similar (Table 4 and supplementary Table 4 in the online appendix).

3.4 Prevalence of IFG and IGT

Interesting, the prevalence of IFG and IGT increased during late puberty and young adult in both sexes and was consistently higher in girls than in boys (Figure 2). Overall, 4.0%, 0.6% and 0% males, and 6.9%, 1.8% and 0.7% females met isolated IFG, isolated IGT and IFG/IGT respectively in this rural Chinese population (the right bottom panel in Figure 2).

3.5 Gender Difference

As show in Figure 1, FPG increased with age till the age of 18 years, and then decreased with age in both sexes. On the other hand, there was a notable gender difference for 2-h PG after early puberty with higher values in female. Females had 0.1 (SE=0.1, $p=0.042$), 0.5 (SE=0.1, $p<0.0001$), and 0.8 mmol/L (SE=0.2, $p<0.0001$) respectively higher 2h PG at early puberty, late puberty and young adult than males. Up to ~12 years of age, log (FSI) and log (2h PI) increased with age in both sexes, but females followed linearly and males followed un-linearly pattern and accelerate during puberty. Log(FSI) returned to pre-puberty at same pattern in males and females, but log(2hPI) decreased slowly in females. Log (HOMA-IR) increased with age and appeared to the peak around the age of 14 years in girls and 16 years in boys, and then returned to pre-puberty levels. Consistently, “U”-shaped QUICKI index across age were observed in both genders, with male lag behind 1–2 years.

4. Discussion

While pubertal IR is well-recognized, little data are on patterns of plasma glucose across childhood, adolescence and young adulthood. This large cohort of twins offered the unique opportunity to investigate the distribution of glucose tolerance, the degree of IR and the timing of occurrence from early childhood to early adulthood in a large rural Chinese population using consistent methods. Therefore, these data provide a useful reference for Chinese children and young adults due to lack of general population data in Chinese. This report contributes new information on glucose tolerance and IR in children and adolescents in several ways. It is one of the first studies to describe age- and gender-specific patterns and distributions of glucose tolerance and IR measures across childhood, adolescence and young adulthood. It also investigates prevalence of IFG and IGT in a large rural Chinese twin population in youth and exposed a clinically unrecognized, high risk group for pre-diabetes. Finally, the results highlight the important difference of gender and pubertal stage on glucose homeostasis and IR and the importance to interpret the measurements in this context.

The results of the present study show that insulin sensitivity appears to be the highest before the onset of puberty, reaches its nadir midway through maturation, and approaches near pre-pubertal levels at the end of maturation. Meanwhile, to maintain glucose homeostasis, pancreatic β -cells compensate for the transient decrease in insulin sensitivity during adolescence by augmenting insulin secretion, leading to a state of chronic hyperinsulinemia after the onset of puberty and improvement in post-puberty. These results are consistent with previous studies [13,14].

Our data show important differences in measures of insulin resistant between males and females with the onset of puberty. First, FSI appeared to peak earlier in girls (around 14

years of age), while FSI peaked at 16 years of age in boys. Similarly, the earlier peak in HOMA-IR levels was seen in girls compared with boys. Second, the gender difference of 2h PI concentrations is more pronounced after onset of puberty. The previous studies in other populations had found the similar results on IR. Moran et al.[13] found higher IR in girls at all Tanner stages in Black and non-Hispanic White. Lee et al.[15] found earlier peak of IR in girls in Mexican American, Black and non-Hispanic White. This gender difference in timing of IR reflects the effect of puberty on IR, as girls experience puberty at an earlier age than boys. However, the underlying biological mechanism of higher 2h PI in female adolescents is not completely clear. This result couldn't be totally due to a greater degree of adiposity in the girls [16]. One study on effects of sex on postprandial glucose metabolism reported that the ability of glucose to enhance its own uptake was greater in the young women and young men [17]. Thereby, potential higher postprandial glucose stimulates greater insulin secretion in females.

In addition, a significant gender difference in glucose tolerance pattern was observed in this population. Females attained higher levels of 2h PG than males and the gender difference became more pronounced with the onset of puberty. This finding is important as females suffer from T2DM much more than males in this age group [4,18]. Indeed, the prevalence of each type of prediabetes was consistently higher in females comparing with males in present study. Previous study found neither differences in overnight growth hormone secretion nor any evidence of differences in peripheral growth hormone responsiveness between sexes [19]. Therefore, the differences in glucose tolerance between the sexes during puberty may be limited to pancreatic beta-cells function and peripheral insulin actions. In adolescence, males have an increase in muscle mass due to testosterone secretion while females have increased body fat mass due to estradiol[20]. This may be a part of reason for sexual dimorphism in plasma glucose distributions. In addition, Basu et al. [17] reported that the ability of glucose to enhance its own uptake was greater and the ability of insulin to stimulate glucose disposal was lower in young women than young men despite lower visceral obesity in the former, indicating that other factors also modulated insulin action. Finally, girls have higher body fat than boys at a given BMI. Obesity is a major risk factor for the development of T2DM [18]. Clinical physiology studies in adults generally, but not unanimously, found that FPG was a better marker of beta-cell dysfunction, whereas 2h PG change was more closely related to insulin-resistant states. Higher 2h PG in females in present study might imply that females had lower tolerance capacity to IR during late puberty and young adult than males of the same age.

As both IFG and IGT, despite representing different physiological alterations, have been shown in adults to predict the development of T2DM, both seem to be worthy of early detection and management. In our study based on a cohort of non-obese rural population in Chinese, below-average BMI and thus reduced diabetes risk, we found a prevalence of individuals with fasting plasma glucose ≥ 7.0 mmol/L and/or 2h post-load glucose ≥ 11.1 mmol/L of 1.8 % and IFG of 3.75% and 6.74% in boys and girls, respectively. Compared with data from National Health and Nutrition Examination Survey (NHANS) 1999–2002, our prevalence data are similar in T2DM and 1.5-fold lower in IFG than in adolescents of a similar age(12–19 years) in the United States[21], and more than 9-fold lower than in a predominantly minority cohort of eight-grade students also in the United States[8]. However, the prevalence data are 3-fold higher than Germany adolescents [22]. The reasons for this difference are not entirely clear, levels of physical activity, dietary habits, socioeconomic status, birth weight and genetics may have led to different degree and time-courses in increase of pre-diabetes and diabetes risk in youth. Difference in the degree of obesity in adolescence was evident when comparing the BMI from the US [23] to our population. We also found increasing prevalence of IFG and IGT with age in both sexes. The rise in the prevalence of IFG and IGT is tightly coupled to the increase of IR during

puberty. In general sense, T2DM is strongly associated with obesity, mainly visceral adiposity, but leanness may place person at low risk for development of T2DM. However, the prevalence of pre-diabetes in our relatively lean population seems above average, which may result from more insulin resistant in twin than singleton [24]. Thus, our data exposed a clinically unrecognized, high risk group for diabetes, which comprises adolescents who are twin girls at 15–20 years of age and are residents of Anqing, China. In addition, transition from IGT to diabetes in adults is usually a gradual phenomenon, occurring over 5–10 years [25,26]. In contrast, Weiss et al. [27] suggested a substantial tempo of deterioration of glucose homeostasis in youth. Therefore, further studies to determine the risk factors for T2DM are of importance in this population.

Potential limitations need to be considered when interpreting our results. Study participants in this study were twins. Previous study reported that twins may be more insulin resistant than singletons [24]. If the impact of twin status existed in this study, the distributions of insulin and HOMA-IR were more likely to shift rightwards to those in non-twin population. However, we do believe that the overall pattern across age and gender should retain in this homogeneous population. Still, caution is needed in generalizing our findings to non-twin and urban Chinese, or other population.

In summary, we observed remarkable pubertal surge of IR and gender difference in this community based, lean rural Chinese sample. Although few subjects had clinically apparent diabetes, there was increasing prevalence of IFG and IGT with age, more so in females. The results emphasize that puberty may be a critical age period for identifying individuals at high risk of developing pre-diabetes. Further following up for this population will determine if pre-diabetes in puberty will develop T2DM in adulthood.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1. Smoothing plots of fasting glucose, 2h post-load glucose, log-transformed fasting serum insulin, 2h post-load insulin and HOMA-IR, and QUICKI against age among 1921 males and 2567 females aged 6–24 years. HOMA-IR, the homeostatic model assessment for insulin resistance; QUICKI, quantitative insulin sensitivity check index.

Figure 2.

The distribution of prediabetes in a rural Chinese non-diabetic adolescents and young adults. IFG, isolated impaired fasting glucose; IGT, isolated impaired glucose tolerance; IFG/IGT, IFG and IGT. Pre-puberty: age <10years; early puberty: 10–14 years; late puberty: 15–19 years, young adult: 20–24years. *P<0.01 compared males.

Table 1

The distributions of fasting glucose by puberty

Age (years)	n	mean	(95%CI) *	SD	Fasting blood glucose (mmol/L)				
					percentiles				
					10th	Median	75th	90th	95th
Male									
Pre-puberty	689	4.4	(4.4 4.5)	0.5	3.8	4.4	4.7	5.1	5.3
Early puberty	794	4.5	(4.5 4.6)	0.5	3.9	4.6	4.9	5.2	5.4
Late puberty	303	4.7	(4.6 4.8)	0.6	3.9	4.7	5.2	5.5	5.8
Young adult	135	4.6	(4.5 4.7)	0.6	3.9	4.6	5.1	5.4	5.7
Female									
Pre-puberty	537	4.3	(4.3 4.4)	0.5	3.7	4.3	4.6	5.0	5.3
Early puberty	742	4.5	(4.5 4.5)	0.6	3.8	4.5	4.8	5.2	5.5
Late puberty	395	4.8	(4.7 4.8)	0.7	3.9	4.7	5.2	5.8	6.0
Young adult	893	4.5	(4.5 4.6)	0.8	3.6	4.4	5.0	5.6	5.9

* 95%CI: 95% confidence interval for the mean, which is calculated based on t distribution.
SD, standard deviations

Pre-puberty: age <10years; early puberty: 10–14 years; late puberty: 15–19 years, young adult: 20–24years

Table 2

The distributions of 2h post-load glucose by puberty.

Age (years)	2-h post-load glucose (mmol/L)								
	n	mean	(95%CI*)	SD	Percentiles				
					10th	Median	75th	90th	95th
Male									
Pre-puberty	650	4.7	(4.6-4.7)	0.9	3.7	4.6	5.2	5.8	6.1
Early puberty	760	4.7	(4.6-4.8)	0.9	3.6	4.6	5.3	5.9	6.2
Late puberty	297	4.8	(4.7-4.9)	1.0	3.6	4.8	5.4	6.1	6.6
Young adult	129	4.6	(4.3-4.8)	1.3	3.0	4.5	5.4	6.1	6.8
Female									
Pre-puberty	511	4.7	(4.6-4.7)	0.8	3.7	4.6	5.1	5.7	6.1
Early puberty	717	4.8	(4.7-4.9)	0.9	3.7	4.8	5.4	6.0	6.3
Late puberty	389	5.3	(5.2-5.4)	1.3	3.8	5.2	6.0	7.0	7.6
Young adult	880	5.3	(5.2-5.4)	1.4	3.7	5.2	6.1	7.1	7.8

* 95%CI: 95% confidence interval for the mean, which is calculated based on t distribution.

SD, standard deviations

Pre-puberty: age <10years; early puberty: 10–14 years; late puberty: 15–19 years; young adult: 20–24 years.

Table 3

The distributions of fasting insulin concentration by puberty.

Age (years)	n	Geometric mean	(95%CI) *	Serum fasting insulin (μU/mL)				
				10th	Median	75th	90th	95th
Male								
Pre-puberty	689	4.9	(4.7 5.2)	2.0	5.0	8.1	12.1	16.1
Early puberty	794	5.8	(5.5 6.1)	2.3	6.1	9.4	13.5	17.3
Late puberty	303	7.3	(6.7 8.0)	2.7	7.9	13.7	19.1	22.5
Young adult	135	5.1	(4.5 5.7)	2.2	4.9	8.1	12.8	18.3
Female								
Pre-puberty	537	5.3	(5.0 5.6)	2.1	5.5	8.2	11.9	16.5
Early puberty	742	6.4	(6.1 6.8)	2.5	6.9	10.8	15.3	19.8
Late puberty	395	6.5	(6.0 7.1)	2.4	6.7	12.2	19.4	25.5
Young adult	893	5.3	(5.0 5.6)	2.0	5.3	9.0	14.1	18.4

* 95%CI: 95% confidence interval for the geometric mean, which is calculated based on t distribution of mean log (serum fasting insulin).
Pre-puberty: age <10years; early puberty: 10–14 years; late puberty: 15–19 years, young adult: 20–24years.

Table 4

The distributions of HOMA-IR by puberty.

HOMA-IR								
Age (years)	n	Geometric mean	(95%CI)*	Percentiles				
				10th	Median	75th	90th	95th
Male								
Pre-puberty	689	0.96	(0.90 1.02)	0.39	0.97	1.59	2.53	3.14
Early puberty	794	1.16	(1.10 1.23)	0.44	1.20	1.91	2.90	3.67
Late puberty	303	1.52	(1.38 1.66)	0.57	1.61	2.97	4.15	4.84
Young adult	135	1.04	(0.91 1.18)	0.41	1.01	1.76	2.83	3.71
Female								
Pre-puberty	537	1.01	(0.95 1.07)	0.38	1.07	1.62	2.41	3.23
Early puberty	742	1.27	(1.20 1.35)	0.48	1.31	2.14	3.24	4.10
Late puberty	395	1.36	(1.24 1.49)	0.46	1.32	2.56	4.09	5.65
Young adult	893	1.04	(0.98 1.10)	0.40	1.06	1.80	2.97	3.73

HOMA-IR, the homeostatic model assessment for insulin resistance;

* 95%CI: 95% confidence interval for the geometric mean, which is calculated based on t distribution of mean log(HOMA-IR).
Pre-puberty: age <10years; early puberty: 10–14 years; late puberty: 15–19 years, young adult: 20–24years.