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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 are available for glucose and insulin pattern from a large, unselected lean population. This report describes the age- and sex-specific distributions of glucose tolerance and IR in a rural Chinese twin population. This report includes 4488 subjects aged 6 to 24 years. The primary variables of interest are fasting plasma glucose, 2-hour postload plasma glucose (2-h PG), fasting serum insulin, 2-hour postload insulin, and the homeostatic model assessment for IR. Age- and sex-specific patterns for the primary variables are described using smoothing plot, arithmetic or geometric mean, and percentiles. There is an increase in fasting plasma glucose, 2-h PG, and IR during puberty (10-19 years) and a return to prepuberty level by the age of 20 years. Insulin resistance peaks at around the age of 14 years in girls and 16 years in boys. Two-hour postload plasma glucose and 2-hour postload insulin are higher in girls than in boys from early puberty, and the sex differences are more pronounced afterward. Moreover, the prevalence of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) increases after puberty and is higher in girls than in boys. In this community-based, nonobese rural Chinese twin population, we observed sex-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 2-h 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 prediabetes.

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 that T2DM in Thai children and adolescents increased from 5% during 1986-1995 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 subclinical 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 and that most patients have impaired glucose regulation, an intermediate stage (prediabetes), 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

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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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 prediabetes 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 prediabetes in children, based on standard values of fasting plasma glucose (FPG), random plasma glucose, and the oral glucose tolerance test (OGTT), are currently the same as in adults [7]. However, compared with epidemiologic data on prediabetes and T2DM in adults, data on the prevalence of T2DM or prediabetes 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 prediabetes or T2DM in children and adolescents is not yet fully understood. The etiology of T2DM in the 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. However, the time course, degree, and sex difference of IR and its contributions to prediabetes or T2DM as children progress through puberty remain 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 3 urban areas and 8 rural counties covering 15 000 km^2. 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 addition, 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 sex- and age-specific patterns and distributions of glucose tolerance and IR during the ages of 6 to 24 years. It also examines the timing of peak IR and investigates the prevalence of prediabetes 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 were 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 3-day workshop in each township to train local physicians 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 physicians 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 physicians. 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 OGTT. Participants were required to fast at least 10 hours before the blood samples were taken. A standard OGTT (1.75 g/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 to 24 years of age. Of a total of 4496, 0.18% (8 individuals) had FPG greater than or equal to 7.0 mmol/L and/or 2-hour postload glucose (2-h PG) greater than or equal to 11.1 mmol/L and were excluded from the final analysis. Four thousand four hundred eighty-eight were included in this report. Of 4488, 155 children have missing data for 2-h PG and 2-hour postload insulin (2-h PI) measurements.

2.2. Laboratory methods

Plasma was separated from blood cell in the field within 30 minutes 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, Tokyo, Japan). Standard quality control procedures were performed each day with standard samples that came with the reagents (coefficient of variation <8%). Serum insulin was measured by electrochemiluminescence method on an Elecsys 2010 system (Roche, Basel, Switzerland). Duplicate analyses were also conducted daily using samples collected from study participants (coefficient of variation <10%, mean = 3%). Insulin resistance was estimated using the homeostatic model assessment for insulin resistance (HOMA-IR) index that was calculated as fasting insulin concentration (in microunits per

milliliter) × fasting glucose concentration (in millimoles per liter)/22.5 [9]. The insulin sensitivity was estimated using the quantitative insulin sensitivity check index (QUICKI) that was calculated as 1/(log fasting insulin concentration [in microunits per milliliter] + log fasting glucose concentration [in milligrams per deciliter]) [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 and 6.9 mmol/L with 2-h PG in OGTT of less than 7.8 mmol/L, and isolated *IGT* is defined as 2-h PG in OGTT of 7.8 to 11.0 mmol/L with FPG less than 5.6 mmol/L. *IFG/IGT* is defined as FPG between 5.6 and 6.9 mmol/L with 2-hour value in OGTT of 7.8 to 11.0 mmol/L.

2.4. Statistical analyses

All analyses were conducted separately by sex using SAS version 9.1 (SAS Institute, Cary. NC). This twin cohort was analyzed as individuals. First, the distributions of age- and sex- specific FPG, 2-h PG, fasting serum insulin (FSI), 2-h PI, and HOMA-IR were examined using arithmetic mean and standard deviation (SD) for glucose measurements, geometric mean for insulin and HOMA-IR, and median and percentiles for all the measurements. We calculated 95% confidence interval (CI) for means. Furthermore, we categorized study individuals into 4 pubertal subgroups based on age—prepuberty (age <10 years), early puberty (10-14 years), late puberty (15-19 years), and young adulthood (20-24 years)—and presented descriptive data for each pubertal group in male and female as well. Comparisons of data among groups were tested by using sex-specific linear regressions. Generalized estimating equations 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 were described using smoothing plots of FPG, 2-h PG, log (FSI), log (2-h PI), log (HOMA-IR), and QUICKI levels by age in both sexes. All smoothing plots used locally weighted nonparametric regression (LOESS) method with SAS procedure LOESS.

3. Results

3.1. Fasting and 2-hour blood glucose

Tables 1 and 2 depict sex-specific means (95% CIs for means); SDs; 10th percentiles; medians; and 75th, 90th, and 95th percentiles for FPG and 2-h PG in the 4 puberty groups. Relative to those at prepuberty, the mean FPG increased at early puberty (β, 95% CI: 0.1, 0.1-0.2, P = .0001 in males; 0.2, 0.1-0.3, P < .0001 in females) and was even higher at late puberty in both sexes (β, 95% CI: 0.3, 0.2-0.4, P < .0001 in males; 0.5, 0.3-0.6, P < .0001 in females). The FPG difference between late puberty and young adulthood was significant in females (0.3, 0.1-0.4, P < .0001), but not in males (0.08, −0.08 to 0.24, P = .337). Supplementary Tables 1 and 2 in the online appendix provide detailed, for each year, age- and sex-specific means (95% CIs for means); SDs; 10th percentiles; medians; and 75th, 90th, and 95th percentiles for FPG and 2-h PG separately. Of note, the 95th percentile values for FPG were greater than 5.6 mmol/L, the cut point for IFG [12], at ages 13 to 21 years in boys and 14 to 24 years in girls. The 2-h PG 95th percentile values were more than 7.8 mmol/L, the cut point for IGT [12], only at ages 21 to 22 years in boys and 18 to 21 years in girls.

3.2. Fasting and 2-hour insulin

Table 3 delineates sex-specific geometric means (95% CIs for means); 10th percentiles; medians; and 75th, 90th, and 95th

Table 1
The distributions of fasting glucose by puberty

Age (y)	Fasting blood glucose (mmol/L)									
	n	Mean	(95% CI)[a]		SD	Percentiles				
						10th	Median	75th	90th	95th
Male										
Prepuberty	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										
Prepuberty	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

Prepuberty: age <10 years; early puberty: 10 to 14 years; late puberty: 15 to 19 years; young adult: 20 to 24 years.
[a] 95% CI for the mean, which is calculated based on t distribution.

Table 2
The distributions of 2-h PG by puberty

Age (y)	2-h PG (mmol/L)									
	n	Mean	(95% CI[a])		SD	Percentiles				
						10th	Median	75th	90th	95th
Male										
Prepuberty	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										
Prepuberty	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

Prepuberty: age <10 years; early puberty: 10 to 14 years; late puberty: 15 to 19 years; young adult: 20 to 24 years.
[a] 95% CI for the mean, which is calculated based on *t* distribution.

percentiles for FSI in the 4 puberty groups. The mean of log (FSI) increased about 0.2 from prepuberty to early puberty (β [SE]: 0.16 [0.05], $P = .0007$ in males; 0.19 [0.05], $P = .0001$ in females), peaked at late puberty (β [SE]: 0.39 [0.07], $P < .0001$ in males; 0.20 [0.06], $P = .0016$ in females), and returned, at young adulthood, to a level that was similar to prepuberty level (0.03 [0.08], $P = .7225$ in males; −0.01 [0.05], $P = .889$ in females). The pattern of 2-h PI across age (middle panels in Fig. 1) was essentially similar to that of FSI.

Supplementary Table 3 in the online appendix delineates, for each year, age- and sex- specific geometric means (95% CIs for means); 10th percentiles; medians; and 75th, 90th, and 95th percentiles for FSI.

3.3. Insulin resistance

Table 4 shows the sex-specific HOMA-IR distributions in the 4 puberty groups. The pattern of log (HOMA-IR) across age was very similar to that for log (FSI) in both sexes (Fig. 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 ages 11 to 14 years (Table 4, Fig. 1). Interestingly, HOMA-IR 95th percentile values for girls surpassed those for boys between 15 and 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

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

3.5. Sex difference

As show in Fig. 1, FPG increased with age until the age of 18 years and then decreased with age in both sexes. On the other hand, there was a notable sex difference for 2-h PG

Table 3
The distributions of fasting insulin concentration by puberty

Age (y)	Serum fasting insulin (μU/mL)								
	n	Geometric mean	(95% CI)[a]		Percentiles				
					10th	Median	75th	90th	95th
Male									
Prepuberty	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									
Prepuberty	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

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

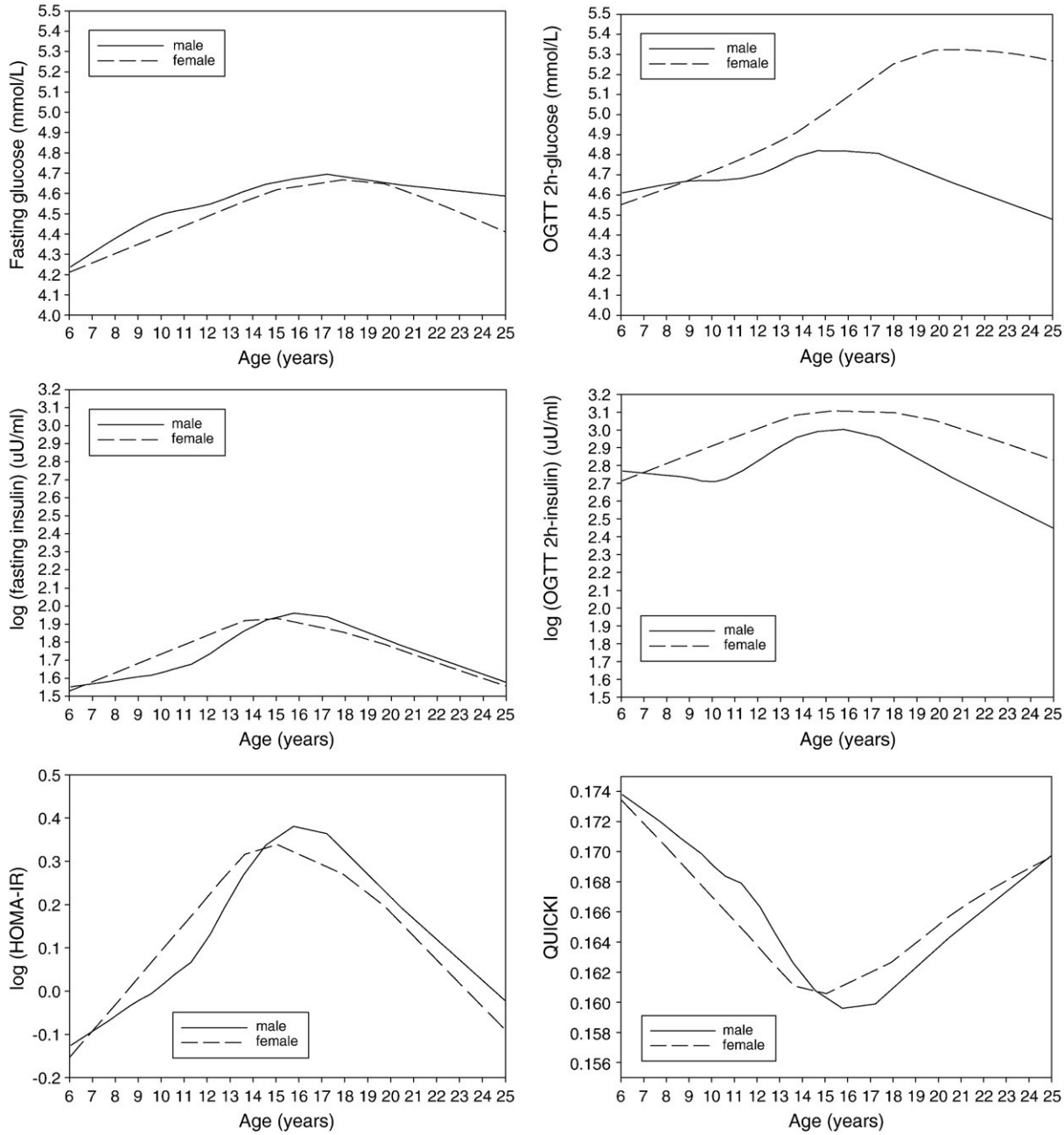

Fig. 1. Smoothing plots of fasting glucose, 2-h PG, log-transferred FSI, 2-h PI and HOMA-IR, and QUICKI against age among 1921 males and 2567 females aged 6 to 24 years. HOMA-IR, the homeostatic model assessment for insulin resistance; QUICKI, quantitative insulin sensitivity check index.

after early puberty, with higher values in females. Females had 0.1 (SE = 0.1, $P = .042$), 0.5 (SE = 0.1, $P < .0001$), and 0.8 mmol/L (SE = 0.2, $P < .0001$), respectively, higher 2-h PG at early puberty, late puberty, and young adulthood than males. Up to about 12 years of age, log (FSI) and log (2-h PI) increased with age in both sexes; but females followed a linear and males followed an unlinear pattern, which accelerated during puberty. Log (FSI) returned to prepuberty at the same pattern in males and females, but log (2-h PI) decreased slowly in females. Log (HOMA-IR) increased with age and appeared to the peak at around the age of 14 years in girls and 16 years in boys, and then returned to prepuberty levels. Consistently, "U"-shaped QUICKIs across age were observed in both sexes, with males lagging behind by 1 to 2 years.

4. Discussion

Although pubertal IR is well recognized, there are little data on patterns of plasma glucose across childhood, adolescence, and young adulthood. This large cohort of

Table 4
The distributions of HOMA-IR by puberty

Age (y)	HOMA-IR								
	n	Geometric mean	(95%CI)[a]		Percentiles				
					10th	Median	75th	90th	95th
Male									
Prepuberty	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									
Prepuberty	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

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

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 because of the 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 sex-specific patterns and distributions of glucose tolerance and IR measures across childhood, adolescence, and young adulthood. It also investigated the prevalence of IFG and IGT in a large rural Chinese twin population in the youth and exposed a clinically unrecognized, high-risk group for prediabetes. Finally, the results highlight the important difference of sex and pubertal stage on glucose homeostasis and IR and the importance of interpreting 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-prepubertal levels at the end of maturation.

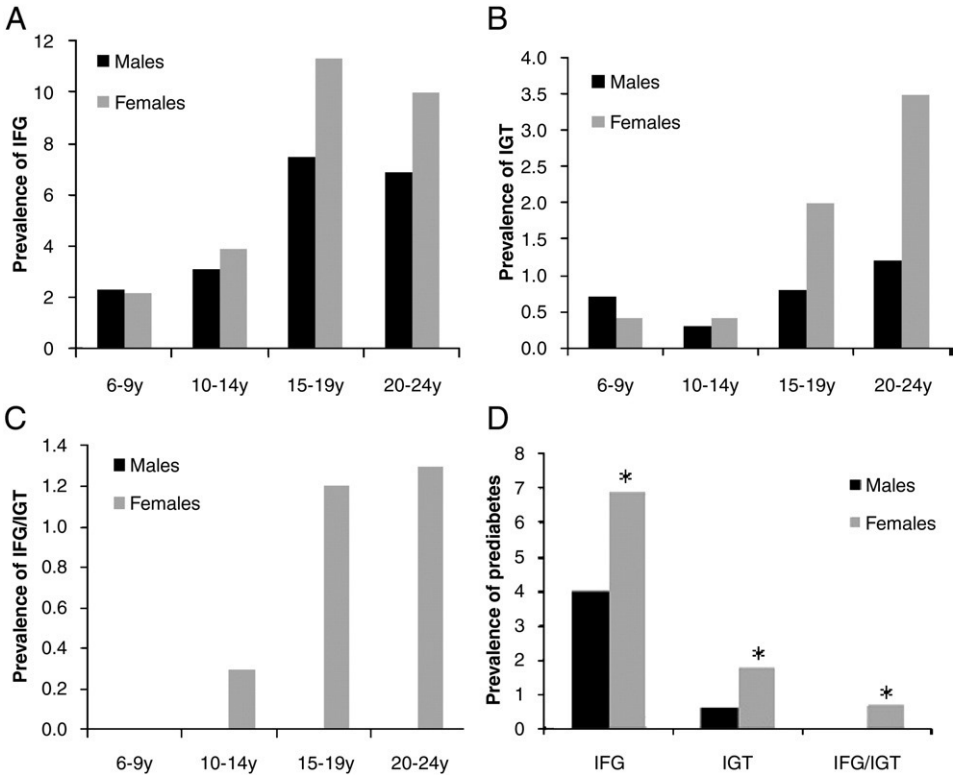

Fig. 2. The distribution of prediabetes in a rural Chinese nondiabetic adolescents and young adults. Prepuberty: age <10 years; early puberty: 10 to 14 years; late puberty: 15 to 19 years; young adult: 20 to 24 years. *$P < .01$ compared with males.

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 postpuberty. 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, an earlier peak in HOMA-IR levels was seen in girls compared with boys. Second, the sex difference of 2-h PI concentrations is more pronounced after the onset of puberty. The previous studies in other populations had found similar results on IR. Moran et al [13] found higher IR in girls at all Tanner stages in black and non-Hispanic white subjects. Lee et al [15] found earlier peak of IR in girls in Mexican American, black, and non-Hispanic white subjects. This sex difference in the 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 2-h PI in female adolescents is not completely clear. This result could not be totally due to a greater degree of adiposity in girls [16]. One study on the effects of sex on postprandial glucose metabolism reported that the ability of glucose to enhance its own uptake was greater in young women than young men [17]. Thereby, potentially higher postprandial glucose stimulates greater insulin secretion in females.

In addition, a significant sex difference in glucose tolerance pattern was observed in this population. Females attained higher levels of 2-h PG than males, and the sex 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 compared with males in the present study. A 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 β-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 the reason for the 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 body mass index (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 β-cell dysfunction, whereas 2-h PG change was more closely related to insulin-resistant states. Higher 2-h PG in females in the 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 physiologic 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 nonobese rural Chinese population with below-average BMI and thus reduced diabetes risk, we found a prevalence of individuals with FPG greater than or equal to 7.0 mmol/L and/or 2-h PG greater than or equal to 11.1 mmol/L of 0.18% and a prevalence of IFG of 3.75% and 6.74% in boys and girls, respectively. Compared with data from the National Health and Nutrition Examination Survey 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 eighth-grade students also in the United States [8]. However, the prevalence data are 3-fold higher than German 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 degrees and time courses in increase of prediabetes 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 a general sense, T2DM is strongly associated with obesity, mainly visceral adiposity; but leanness may place a person at low risk for development of T2DM. However, the prevalence of prediabetes in our relatively lean population seems to be above average, which may result from more insulin resistance in twins than singletons [24]. Thus, our data exposed a clinically unrecognized, high-risk group for diabetes, which comprises adolescents who are twin girls at 15 to 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 to 10 years [25,26]. In contrast, Weiss et al [27] suggested a substantial tempo of deterioration of glucose homeostasis in the 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. A 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 rightward to those in nontwin populations. However, we do believe that the overall pattern across age and sex should be retained in this homogeneous population. Still, caution is needed in generalizing our findings to nontwin, urban Chinese, or other populations.

In summary, we observed a remarkable pubertal surge of IR and sex 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 prediabetes. Further follow-up for this population will determine if prediabetes in puberty will develop T2DM in adulthood.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.metabol.2010.04.022.

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