



ORIGINAL ARTICLE

Association of body mass index with serum alanine aminotransferase in Chinese adolescents: a school-based cross-sectional study

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Abstract

Background: Numerous studies have consistently demonstrated that high body mass index (BMI) is related to elevated serum alanine aminotransferase (ALT) among adults, but little is known about the association regarding adolescents, especially in China. In this study, we aimed to investigate the association between BMI and ALT activity among Chinese adolescents.

Methods: A school-based cross-sectional study was performed among nine high schools in Shenzhen, China between February 2017 and June 2018. A generalized linear-regression model adjusting for age and gender was conducted, and bivariate correlation analysis between ALT and BMI was also performed.

Results: A total of 7,271 adolescents aged from 9 years to 17 years were enrolled. Height, weight, BMI, and ALT were higher among boys than among girls (all $P < 0.001$). The mean (standard deviation) of serum ALT levels was 14.26 (14.77) U/L. In the entire BMI range, the BMI–ALT correlation was stronger for boys (Spearman's $r = 0.396$, $P < 0.001$) and adolescents of 14 years–17 years ($r = 0.356$, $P < 0.001$) than for girls ($r = 0.203$, $P < 0.001$) and adolescents of 9 years–13 years ($r = 0.221$, $P < 0.001$), respectively. Serum ALT increased rapidly and followed a linear pattern from the point of $\text{BMI} \geq 20.5 \text{ kg/m}^2$, and each increase of 1 kg/m^2 in BMI range above 20.5 kg/m^2 was averagely correlated with an increase of 2.71 U/L in ALT levels ($P < 0.001$).

Conclusions: We found a significant BMI–ALT relationship. BMI at 20.5 kg/m^2 may be a cut-off for evaluating serum ALT. BMIs $\geq 27.1 \text{ kg/m}^2$ for boys and $\geq 24.9 \text{ kg/m}^2$ for girls were linked to an elevated ALT activity for Shenzhen adolescents.

Key words: adolescent; alanine aminotransferase; association; body mass index; cut-off point

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Introduction

The laboratory parameter of serum alanine aminotransferase (ALT) is widely used as a sensitive surrogate marker of a variety of liver diseases (e.g. nonalcoholic fatty liver disease) and elevated serum ALT levels are closely related to liver-fat accumulation [1–4]. Overweight or obesity is also a risk factor for the elevation of serum liver enzymes, reflecting hepatic damage [5, 6]. Recent epidemiological findings have pointed out that both high body mass index (BMI) and elevated ALT were strongly associated with a range of poor health outcomes such as insulin resistance and type 2 diabetes, metabolic disorders (e.g. high blood pressure, increased visceral fat, hyperlipidemia, and metabolic syndrome), and cardiovascular and cerebrovascular diseases [7–12]. Gaining an insight into the relationship between BMI and serum ALT levels is indispensable.

Numerous pieces of cross-sectional epidemiologic and clinical research have consistently demonstrated that high BMI was related to an elevation of ALT concentrations among adults [4–6, 13–16]. For example, according to the degree of BMI from a total of 3,098 Korean adults, the unadjusted odds ratio (OR) and 95% confidence interval (CI) for elevated ALT concentration statistically increased among men (1.90 [1.25–2.93] for the $23 \leq \text{BMI} < 25 \text{ kg/m}^2$ group and 5.01 [3.49–7.21] for the $\text{BMI} \geq 25 \text{ kg/m}^2$ group) and women (2.44 [1.24–4.82] and 3.94 [2.18–7.13], respectively), as compared to the $\text{BMI} < 23 \text{ kg/m}^2$ group [17]. However, little information on the association between BMI and ALT among adolescents is available to date [18, 19], especially in China. The relationship among adolescents might differ from that among adults. Thus, the aim of the present study was to investigate the association between BMI and the concentration of serum ALT among Chinese adolescents.

Materials and methods

Study design, data collection, and measures

Between February 2017 and June 2018, we carried out a school-based cross-sectional study that enrolled all freshmen from nine separate junior and senior high schools in the Baoan District of Shenzhen, China, based on the compulsory admission physical examination organized by the Baoan District Government of Shenzhen. Written informed consents for each study participant and their parents were dutifully obtained. Students who were aged between 9 years and 17 years were considered adolescents in the present study.

Anthropometric measurements of standing height and weight were measured by trained physicians to the nearest 0.5 cm and 0.1 kg, respectively, with the participants in lightweight clothing and without shoes; BMI was calculated by dividing the weight (in kilograms) by the square of the height (in meters). Individual characteristic data such as name, class and grade, date of birth (i.e. age), and gender for each student were also collected to set up an original database. Fasting blood samples were drawn from an antecubital vein into vacutainer tubes by trained nurses on the morning after the study participants had fasted for at least 10 hours overnight. The samples were subsequently delivered to the hospital laboratory by a specially assigned physician and centrifuged within 1 hour. ALT was measured using the AU5800 serial with the fully automatic biochemical analyser (specification models: Model AU5821, Tokyo, Japan; Product standard number: YZB/JAP 3087–2011) by the manufacturing enterprise of Beckman Coulter K.K.

Statistical analysis

Histograms of BMI and serum ALT levels were displayed. In the specific subgroups analyses, all adolescent students were divided into

four BMI-subgroups (<18.5 , $18.5\text{--}22.9$, $23.0\text{--}24.9$, and $\geq 25.0 \text{ kg/m}^2$) according to the Asia-Pacific classification of BMI [20] as well as 18 BMI-subgroups (≤ 14.9 , $15.0\text{--}30.9$ separated by a distance of 1 kg/m^2 , and $\geq 31.0 \text{ kg/m}^2$) for further comparisons, two age-subgroups (aged 9 years–13 years and 14 years–17 years), and two gender-subgroups (boys and girls) to quantitatively estimate the association of ALT with BMI. BMI was appropriately treated as a continuous variable or an ordinal variable. A generalized linear-regression model adjusting for age and gender as covariates was conducted to reflect the exposure–response effect of BMI with ALT levels, with a natural cubic spline with 4 degrees of freedom (*df*) for BMI to control the inherently non-linear patterns [21]. Spearman's rank bivariate correlation analysis between ALT and BMI was also performed. Based on the exposure–response curve of BMI–ALT in our preliminary analysis, a two-piecewise-linear threshold function, a simple 'hockey-stick' model [22], was conducted, because we found that the concentrations of serum ALT remain unchanged below a BMI threshold of 20.5 kg/m^2 and dramatically and linearly increased with $\text{BMI} \geq 20.5 \text{ kg/m}^2$. All figures and statistical analyses involved the use of R version 3.5.1 (<http://www.R-project.org>) and two-tailed *P*-values < 0.05 were considered statistically significant.

Results

Sample descriptive characteristics

A total of 7,382 adolescents first agreed to participate in our survey. We excluded 81 students due to missing data on age, height, weight, or ALT values; 30 participants with age ≥ 18.0 years or age < 9.0 years were also excluded due to the small sample size in those age groups and that we only focused on adolescents but not adults, preadolescents, or children. The final sample in the present study consisted of 7,271 adolescents aged 9–17 years for the effective statistical analysis and involved 4,014 (55.2%) boys, 3,257 (44.8%) girls; 3,011 (41.4%) participants were aged 9 years–13 years and 4,260 (58.6%) were aged 14 years–17 years.

Boys had higher height, weight, BMI, and ALT than girls (all $P < 0.001$), with no statistical difference in age (Table 1). Table 2 summarizes baseline data of the study participants for the

Table 1. Baseline characteristics of the 7,271 participants of Shenzhen, China, 2017–2018

Variable	Total adolescents (<i>n</i> = 7,271)	Boys (<i>n</i> = 4,014)	Girls (<i>n</i> = 3,257)	<i>P</i> -value*
Age, years	14.2 ± 1.8	14.2 ± 1.8	14.2 ± 1.8	0.518
Height, cm	165.1 ± 9.2	167.7 ± 9.7	161.8 ± 7.5	<0.001
Weight, kg	55.0 ± 12.6	57.5 ± 14.0	51.9 ± 9.8	<0.001
BMI, kg/m ²	20.0 ± 3.6	20.3 ± 3.9	19.7 ± 3.1	<0.001
ALT, U/L	14.3 ± 14.8	15.9 ± 17.0	12.1 ± 11.1	<0.001
Categories of age				0.106
9–13 years	3,011 (41.4%)	1,696 (42.3%)	1,315 (40.4%)	
14–17 years	4,260 (58.6%)	2,318 (57.7%)	1,942 (59.6%)	
Asia-Pacific categories of BMI				<0.001
<18.5	2,753 (37.9%)	1,510 (37.6%)	1,243 (38.2%)	
18.5–22.9	3,328 (45.8%)	1,736 (43.2%)	1,592 (48.9%)	
23.0–24.9	519 (7.1%)	294 (7.3%)	225 (6.9%)	
≥25.0	671 (9.2%)	474 (11.8%)	197 (6.0%)	

Data are expressed as mean ± standard deviation or number (%). ALT, alanine aminotransferase; BMI, body mass index.

**P*-value for comparing girls with boys by Mann–Whitney U test for the variables with skewed distributions, or by Pearson's chi-square test for categories of age and BMI; the bold text indicates a statistical significance.

Table 2. Baseline descriptive statistics for serum ALT (U/L) levels by gender-, age-, and BMI-subgroups among the adolescents of Shenzhen, China, 2017 – 2018

Categories	N	Mean	SD	Min.	Percentiles					Max.
					25th	50th	75th	90th	95th	
Total adolescents	7,271	14.26	14.77	1	9	11	15	21	30	495
Gender										
Boys	4,014	15.94	17.01	1	10	12	16	25	37	495
Girls	3,257	12.18	11.07	1	9	10	13	17	22	415
Categories of age										
9 – 13 years	3,011	12.82	11.57	1	9	11	14	18	22	415
14 – 17 years	4,260	15.28	16.59	1	9	11	16	24	34	495
Asia-Pacific categories of BMI										
<18.5	2,753	11.53	7.10	1	9	10	13	16	19	206
18.5 – 22.9	3,328	12.66	6.85	1	9	11	14	19	23	82
23.0 – 24.9	519	17.45	14.49	4	11	14	19	28	38	189
≥25.0	671	30.90	37.89	3	14	20	33	57	89	495

ALT, alanine aminotransferase; BMI, body mass index; Min., minimum; Max., maximum; N, number; SD, standard deviation.

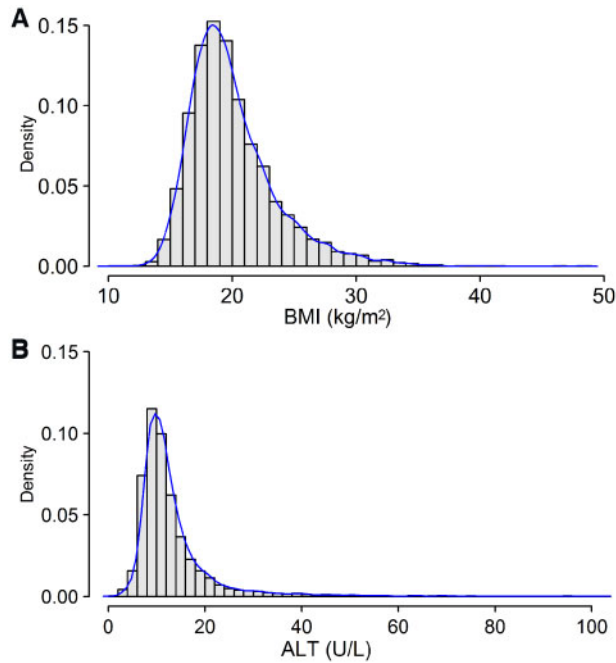


Figure 1. Histograms of body mass index (BMI; panel A) and serum alanine aminotransferase (ALT; panel B) levels among the adolescents (aged 9 years–17 years) of Shenzhen, China, 2017 – 2018

concentrations of serum ALT stratified by gender, age, and BMI. Overall, the mean (standard deviation) of the serum ALT levels was 14.26 (14.77) U/L, with a maximum value of 495.0 U/L. According to the 18 BMI-subgroups, baseline statistics among the total adolescents and gender- and age-subgroups for ALT activity are also shown in [Supplementary Tables 1–3](#). [Figure 1](#) displays the histograms of BMI values and ALT activity.

BMI-ALT association

[Figure 2](#) shows the mean of the serum ALT levels based on BMI stratified by gender and age. When the BMI value was <21 kg/m², the mean of the ALT levels had nearly the same values regardless of gender and age; with BMI ≥21 kg/m², the ALT greatly increased with increasing BMI and peaked in the two highest

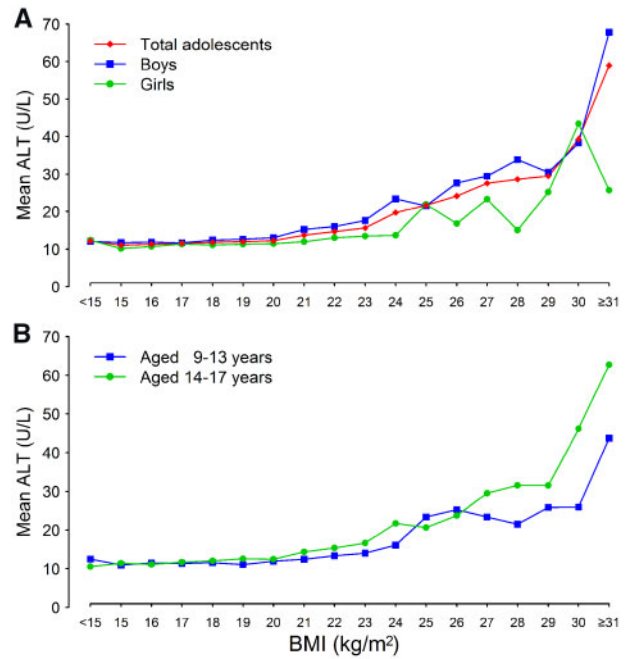


Figure 2. The mean level of ALT (U/L) based on BMI stratified by gender (panel A) and age (panel B) among the adolescents of Shenzhen, China, 2017 – 2018

strata of BMI for the total study subjects and all subgroups. The concentration of serum ALT was higher for boys and adolescents aged 14–17 years than for girls and adolescents aged 9–13 years, respectively. The BMI-ALT relationship curve in [Figure 3](#) visually demonstrates a significant and approximate linear increase in ALT effect in the range of BMI above the threshold of 20.5 kg/m², while the left section was constrained to a zero slope (i.e. a constant for the level of serum ALT).

Bivariate correlation analysis

[Table 3](#) presents the Spearman’s rank correlation coefficients between ALT and BMI. In the entire BMI range, the results indicated that individual ALT levels were positively correlated with BMI ($r = 0.203\text{--}0.396$, all $P < 0.001$). Among the patients with BMI <20.5 kg/m², the correlations of BMI with ALT levels were very

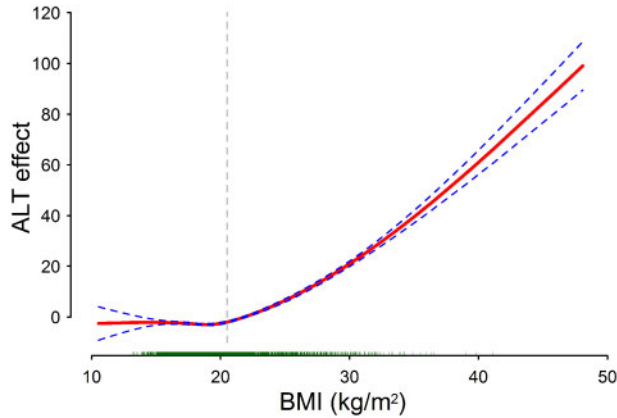


Figure 3. The exposure–response effect (with 95% confidence interval) between ALT and BMI, based on a generalized linear-regression model adjusting for age and gender as covariates. The vertical dotted line was the threshold of 20.5 kg/m², and the levels of serum ALT dramatically and linearly increased above the cut-off point of BMI.

Table 3. Spearman’s rank correlation coefficients between ALT and BMI in the overall study population and stratified by gender and age

Population	Entire BMI		BMI <20.5 kg/m ²		BMI ≥20.5 kg/m ²	
	r	P	r	P	r	P
Total adolescents	0.309	<0.001	0.050	0.001	0.418	<0.001
Boys	0.396	<0.001	0.063	0.002	0.477	<0.001
Girls	0.203	<0.001	0.056	0.008	0.292	<0.001
Aged 9 – 13 years	0.221	<0.001	−0.004	0.859	0.387	<0.001
Aged 14 – 17 years	0.356	<0.001	0.090	<0.001	0.435	<0.001

ALT, alanine aminotransferase; BMI, body mass index.

weak ($r = -0.004$ to 0.090). In contrast, among the patients with BMI ≥ 20.5 kg/m², the BMI–ALT correlation was more pronounced and turned stronger, with a higher coefficient of 0.418 for the total adolescents, 0.477 for boys, 0.292 for girls, 0.387 for adolescents aged 9 years–13 years, and 0.435 for adolescents aged 14 years–17 years (Table 3). Overall, the BMI–ALT correlation coefficients were relatively higher in patients with BMI ≥ 20.5 kg/m² than in those with BMI < 20.5 kg/m².

A sensitivity analysis was carried out to check the stability of our main findings by removing the outliers of serum ALT levels (ALT ≥ 100 U/L; $n = 32$). All of the ALT–BMI correlations were robust, and most coefficients remain unchanged (Supplementary Table 4).

A piecewise threshold function for curve fitting

In view of the exposure–response curve and the correlation coefficients from our previous analyses (Figure 3 and Table 3), we carried out a ‘hockey-stick’ model to assess the curve fitting. To maintain the robustness and generalization of our findings, we restricted the analysis among adolescents with BMI values from 14.0 to 34.9 kg/m², as the sample size was too small for patients with BMI < 14 kg/m² ($n = 11$) and those with BMI ≥ 35 kg/m² ($n = 16$). The two-piecewise-linear threshold function was as follows:

$$ALT = \begin{cases} 11.71 & 14 \leq BMI < 20.5 \\ -62.93 + 1.03 \times Age + 5.16 \times Gender + 2.71 \times BMI & 20.5 \leq BMI < 35 \end{cases}$$

Table 4. An adolescent diagnosed with elevated ALT (>30 U/L for boys and >19 U/L for girls) linked to age and BMI

Age, years	BMI, kg/m ²	
	Boys	Girls
9.0 – 9.9	29.0	26.8
10.0 – 10.9	28.6	26.5
11.0 – 11.9	28.2	26.1
12.0 – 12.9	27.8	25.7
13.0 – 13.9	27.5	25.3
14.0 – 14.9	27.1	24.9
15.0–15.9	26.7	24.6
16.0 – 16.9	26.3	24.2
17.0 – 17.9	26.0	23.8

ALT, alanine aminotransferase; BMI, body mass index.

In the above equation, girls = 0 and boys = 1 for Gender; 9 years, 10 years, 11 years, 12 years, 13 years, 14 years, 15 years, 16 years, or 17 years for Age. The curve of the BMI–ALT relationship can be adequately approximated by the piecewise threshold function model. In the range of $20.5 \leq BMI < 35$ kg/m², residual standard error = 20.31, $df = 2,570$, $adjust-R^2 = 0.1803$, and $P < 0.001$. An increase of 1 kg/m² in BMI above an obesity index of 20.5 kg/m² was averagely associated with an increase of 2.71 U/L in the concentration of serum ALT.

In the clinical practice for adolescents, a boy with ALT >30 U/L and a girl with ALT >19 U/L were usually regarded as having an elevated serum ALT concentration (i.e. a diagnosis of abnormal ALT) [2, 23, 24]. Thus, with an average age of 14 years among adolescents, by calculating backwards using the above mathematical formula, we can estimate that boys with BMI ≥ 27.1 kg/m² and girls with BMI ≥ 24.9 kg/m² were linked to the diagnosis of an elevated level of serum ALT (Table 4).

Discussion

The present study addressed the relationship between BMI and the concentration of serum ALT, based on a school-based observational study of 7,271 Chinese general adolescents aged from 9 years to 17 years. Boys and adolescents aged 14 years–17 years had higher ALT levels than girls and the younger group, respectively. Results of our study also presented higher coefficients of BMI–ALT correlation among boys and adolescents aged 14 years–17 years. These findings specifically indicated that the ALT levels rapidly, linearly, and significantly increased in the range of BMI >20.5 kg/m², suggesting that weight reduction might lower the BMI-associated elevations of liver-function tests.

Our results were in agreement with previous studies that suggested a strong positive relationship between BMI and serum ALT activity [5, 6, 13, 15, 25, 26]. The viewpoint of the ALT elevation connected to the increase in BMI was adequately emerged among adults [25, 26]. Evidence of obesity-related liver injury in the Western Australian general population has shown that overweight (BMI 25–29.9 kg/m²) and obese (≥ 30 kg/m²) residents separately had a significantly 2- to 3-fold and 7-fold increased odds risk for an elevated ALT concentration, as compared to normal-weight subjects (18–24.9 kg/m²), adjusting for age and alcohol ingestion in a multivariate logistic-regression model [27]. Similarly, among non-diabetic Korean adults aged 20 years or more, obesity measured by BMI was an independent and strong indicator of elevated ALT activity, with an

adjusted-OR of 1.55 (95% CI, 0.65–3.68) to 3.47 (95% CI, 2.26–5.33) for obesity or overweight in both sexes, respectively, after adjustment for other putative risk factors [17].

A new insight from the perspective of graphical data for the BMI-ALT curve from our observational research showed a significant increase in BMI above the threshold of 20.5 kg/m², which suggested that a BMI of 20.5 kg/m² may be an important cut-off for predicting higher levels of ALT for the local adolescents of Shenzhen, China. We also adequately fitted a two-piecewise threshold function to predict the concentration of serum ALT with the significant predictors of age, gender, and BMI, speculating that each increase of 1 kg/m² in the BMI range above 20.5 kg/m² was averagely linked to an increase of 2.71 U/L in ALT levels, and BMIs ≥ 27.1 kg/m² for boys and ≥ 24.9 kg/m² for girls were linked to a diagnosis of abnormal ALT. Typically, Lawlor et al. [16] have indicated that BMI was positively and linearly allied to ALT among British women: a one-standard-deviation increase in the BMI value was independently associated with a 0.46-U/L (95% CI, 0.16–0.75) increase in ALT, based on an adjusted linear-regression model with data from the British Women's Heart and Health Study, 1999–2001. To conclude that the thresholds of 27.1 kg/m² for boys and 24.9 kg/m² for girls in BMI are responsible for elevating ALT, further evidence is needed to confirm by prospective cohorts.

For adolescents, positive correlations between serum ALT levels and obesity indices (e.g. body-fat percentage, total fat mass, waist circumference, waist-to-height ratio, BMI, and BMI z-score) were substantially demonstrated in recent studies [14, 18, 19, 28]. Results based on 2,499 school children (aged 9 years or 10 years) from elementary schools in Japan during 2004–2009 showed that the BMI-ALT correlation coefficient was higher for boys than for girls (Spearman's $r=0.353$ vs 0.235) [29]. In Korean adolescents aged 10–18 years, Ahn and co-workers also found a higher positive correlation coefficient among boys ($r=0.555$, $P<0.0001$) than girls ($r=0.162$, $P=0.0086$), based on data derived from the 2010–2011 Korean National Health and Nutrition Examination Surveys [19]. Our study showed analog and positive coefficients in both the entire BMI range (0.396 for boys and 0.203 for girls) and BMI ≥ 20.5 kg/m² areas (0.477 for boys and 0.292 for girls). We also found that higher BMI-ALT correlations for adolescents of 14–17 years than adolescents of 9–13 years.

Several limitations of the present study should be pointed out. First, as our findings were based on a cross-sectional design, we were unable to determine whether there was a causal relationship between BMI and ALT concentration. Thus, the obtained associations in this study should be considered with caution [14, 17]. Second, other potentially important confounders (e.g. physical activity, sedentary behavior, coffee and alcohol consumption, smoking, food intake, and family socioeconomic position and living settings), which might have an impact on chronic diseases or known to be related to enhanced ALT, were not under our consideration [6, 14, 17]. However, based on a random sample of 3,789 British women aged 60–79 years, Lawlor et al. [16] found that the linear BMI-ALT association was independent of alcohol intake, smoking, physical activity, and childhood and adulthood socioeconomic position, as demonstrated in stratified and multivariable analyses. Another limitation was the omission to measure some important obesity indices (e.g. waist circumference, hip circumference, body-fat percentage, abdominal height, and the subsequent composite indicators of waist-to-hip ratio and waist-to-height ratio), which might be connected to the level of serum ALT concentration. With a random

sample of 2,704 indigenous adult residents of New York State, a population-based study by Stranges et al. [28] on the relationships of central-fat accumulation with liver-function tests had pointed out that, followed by BMI, abdominal height, measured by the Holtain-Kahn abdominal caliper, was the most powerful independent predictor of ALT in multivariate models for both sexes. We highly recommended that several large-scale follow-up studies involved with some biopsy-proven samples should be conducted in the future to discover the mechanism behind overweight and obesity, and the potentially causal effects on an elevated ALT concentration.

Conclusions

In conclusion, our study found a significant relationship between BMI and ALT regarding Chinese adolescents. Higher coefficients of BMI-ALT correlation were shown among boys and adolescents of 14–17 years. The concentration of ALT rapidly and significantly increased in BMI ≥ 20.5 kg/m², meaning that a BMI of 20.5 kg/m² may be an important cut-off to evaluate ALT, and boys with BMI ≥ 27.1 kg/m² and girls with BMI ≥ 24.9 kg/m² were connected to an elevation of serum ALT for Shenzhen adolescents.

Supplementary Data

Supplementary data is available at *Gastroenterology Report* online.

Authors' contributions

H.Z. and Z.D. conceived of and designed the experiments. J.Z., C.Y.D., and Y.B.Y. collected and cleaned the data. Z.D. drafted the manuscript. Z.D. and H.Z. revised the manuscript and interpreted the results. All authors read and approved the final manuscript.

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Conflicts of interest

The authors declare that they have no competing financial interests.

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