Original Article

Serum vitamin A status is associated with obesity and the metabolic syndrome among school-age children in Chongqing, China

Xiaoping Wei MD^{1,2,3,4}, Rong Peng MD^{1,4}, Jiaoyang Cao MD^{1,4}, Yu Kang PhD^{2,3,4}, Ping Qu MD^{2,3,4}, Youxue Liu PhD^{1,2,3,4}, Xiaoqiu Xiao PhD^{2,3,4}, Tingyu Li MD^{1,2,3,4}

¹Children's Nutrition Research Center, Children's Hospital of Chongqing Medical University, Chongqing, PR China

²Ministry of Education Key Laboratory of Child Development and Disorders, Children's Hospital of Chongqing Medical University, Chongqing, PR China

³Chongqing International Science and Technology Cooperation Center for Child Development and Disorders, Children's Hospital of Chongqing Medical University, Chongqing, PR China

⁴Key Laboratory of Paediatrics in Chongqing, Children's Hospital of Chongqing Medical University, Chongqing, PR China

The aim of our study was to examine the association of vitamin A status with obesity and the metabolic syndrome (MS) in school-age children in Chongqing, China. A cross-sectional study was conducted of 1,928 children aged 7~11 years from 5 schools in Chongqing, China. Body height, weight, waist circumference (WC) and blood pressure were measured. Blood glucose, lipids and vitamin A were determined. Overall prevalences for overweight, obesity and MS were 10.1%, 6.7% and 3.5%, respectively. There were 274 (14.2%) marginally vitamin A deficient (MVAD) children and 53 (2.8%) vitamin A deficient (VAD) children, respectively. Serum vitamin A in the obese group was significantly lower than in the overweight and normal weight groups (p<0.001). Body mass index (BMI), WC, high density lipoprotein cholesterol (HDL-C) and glucose were strongly associated with vitamin A status (p<0.05). In a separate model adjusted for age and sex, compared with normal children, participants with obesity had a significantly higher risk of having vitamin A insufficiency (\leq 1.05 µmol/L) (OR: 2.37; 95% CI: 1.59, 3.55) (p<0.001), and participants with MS had a 1.99-fold (95% CI: 1.14, 3.47) greater risk of having vitamin A insufficiency (p=0.016), while participants with VAD had significantly higher risk of having MS (OR: 3.82; 95% CI: 1.44, 10.2) (p=0.007). Vitamin A insufficiency among Chongqing urban school-age children was found to be a severe health problem, significantly associated with obesity, hypertriglyceridemia and MS.

Key Words: vitamin A, metabolic syndrome, obesity, school-age children, body mass index

INTRODUCTION

Overweight and obesity have emerged as a global public health concern, threatening many regions of the world, and the prevalence of overweight and obesity is still on the rise worldwide among both adults and children.¹ According to the report of Després J-P et al, obesity is a major risk factor for angiocardiopathy and the conjunction of hypertension, diabetes and dyslipidemia, which are reflected in the metabolic syndrome (MS), potentially imperiling future public health.² Rapid urbanization and economic development in China have led to new patterns of life with over-nutrition and less physical activity, resulting in high prevalences of obesity and MS.³ Chronic non-communicable diseases in adults are linked to energy dysregulation in childhood. In particular, and of public health relevance, these childhood metabolic abnormalities are associated with central obesity in children and adults.⁴

Malnutrition and over-nutrition coexist worldwide representing not only problems of energy regulation, but also of dietary quality. Low calcium intakes and low vitamin D status may be linked to obesity,⁵ as may other indices of dietary quality.⁶ A better understanding of the relationship between nutrient deficiency and obesity is required .

Vitamin A is a micronutrient required for growth and development, conceivably affecting energy regulation and body composition. Vitamin A deficiency (VAD) is one of the more common childhood health problems in developing countries.⁷ Lin LM et al showed that VAD is to be found in Chinese children, especially in remote and poverty-stricken rural areas where food-based approaches or,

Corresponding Author: Dr Tingyu Li, Children's Nutrition Research Center, Children's Hospital of Chongqing Medical University, No.136 Zhongshan Er Road Yuzhong District, Chongqing 400014, PR China.

Tel: +86(023)6363 8660; Fax: +86(023)6362 6904 Email: tyli@vip.sina.com

Manuscript received 30 November 2014. Initial review completed 14 April 2015. Revision accepted 07 May 2015. doi: 10.6133/apjcn.092015.03 depending on circumstances, vitamin A supplementation is needed for the children.⁸ Low concentrations of serum retinol have been found in overweight and obese individuals.9 A negative correlation has also been found between the serum retinol and weight, body mass index (BMI), and hip circumference in overweight and obese Thai adults in a case-controlled study.¹⁰ However, most of such studies have been performed in adults, with relatively few reports of the relationship between VAD and metabolic abnormalities among children. Therefore, the aim of our study was to examine whether vitamin A status is associated with the prevalence of obesity and MS among school-age children in Chongqing, China. We performed physical measurements and determined blood glucose, lipids and vitamin A in 1,928 children aged 7~11 years from 5 schools in Chongqing, China so that we could examine the relationship between metabolic risk factors and the vitamin A status.

MATERIALS AND METHODS

Participants and setting

Multistage cluster random sampling was used in the current study. In the first stage, Yuzhong District of Chongging was randomly chosen from 9 main urban districts of Chongqing. In the second stage, 5 primary schools were randomly chosen from 29 primary schools of Yuzhong District. Then, each 2 classes from Grade 1-5 of the 5 schools were randomly chosen, and all the children in each class were recruited. A total of 2033 children were recruited. We then excluded the children who do not conform to the eligible criteria. The eligible criteria for participation were as follows: 1) Children who had no chronic diseases, including organic cardiovascular diseases, endocrine diseases, liver and kidney diseases, diarrhea and infection diseases, including pneumonia, upper respiratory infection and influenza. 2) Children who had not been recently taking in large doses of vitamin A. 3) Children whose parents or guardians signed and returned consent (written) to participate in all aspects of the study. Finally, a total of 1,928 subjects conformed to the eligible criteria.

We calculated the sample size based on the reported prevalence of metabolic syndrome in adolescents of China.¹¹ Given that the morbidity of MS (P) was approximately 3.2% among children in this population, the sample size was estimated to achieve that percentage with an error (δ) lower than 1%. Statistical significance (α) was set at 0.05 (two-sided). The minimum sample size, based on the calculation formula, which is N=[U² α ×P×(1-P)]/ δ^2 , consistent with this error was 1,190 children. Considering that some children may not conform to the inclusion criteria, a total of 2,033 children were recruited, and the final number of the investigated subjects was 1,928 after exclusion. The sample size was large enough.

Physical examination

The body height and weight were measured by the trained investigators according to the unified criterion. When measuring the weight, students only wore underwear and the results were to an accuracy of 0.1 kg. Metal column height-measure was used to measure the height. When measuring the waist circumference (WC), the subjects

were required to stand upright, relax the waistbands, part legs and let both arms around the chest. The height and WC were valued at end-expiratory as the level of the midpoint connected by the low margin of the middle axillary line ribs and the superior margin of the iliac crest. The values of height and WC were accurate to 0.1 cm. BMI=weight/height² (kg/m²). Mercury sphygmomanometer was used to measure the blood pressure, and five minutes' rest was given before test, and the right arm was measured with the first sound of Korotkoff as systolic blood pressure (SBP) and the fifth sound as diastolic blood pressure (DBP).¹² The average values of two measurements with the same method were calculated and recorded. If the difference of the two blood pressure values was more than 10 mm Hg, the third blood pressure value would be measured, calculated the last two average values, and then the record will be taken.

Blood indexes measurement

With the signed informed consent, about 5 mL fasting venous blood of each subject was extracted. Total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and fasting blood glucose (FPG) levels in serum were determined after centrifugation. TC, TG, HDL-C, and LDL-C levels were detected by automatic biochemical analyzer, and the reagent was purchased from Randox Laboratories Ltd. FPG was determined with Glucose-Hexokinase. Reversed phase high-performance liquid chromatography (HPLC) was used to measure the serum level of vitamin A. The system includes Waters 2487UV detector (USA), 1,525 double-pump, Breeze color spectrum workstation and Symmetry Shield RP18 3.9×150 mm chromato bar. Chromatographic condition: mobile phase: methyl alcohol vs water =95 vs 5, flow rate: 1.4 mL/min, wave length: UV315 nm, retention time 3.5 min.¹³

Definition of outcomes

The screening BMI value classified criterion on overweight and obesity in school-age children was recommended by Working Group on Obesity in China (WGOC).¹⁴ Since the school-age children were still in the process of growing up, we took age and sex into consideration in the nutritional status assessment by BMI. For those children at the same age and sex, when their BMIs were higher than the BMI critical value of the overweight (85th percentile) and lower than the BMI critical value of the obesity (95th percentile), they were overweight; if their BMIs were higher than 95th percentile, they were obese. Currently, the criteria have been extensively applied to judge overweight and obese school-age children in China. In view of no unified diagnosis criteria on MS in school-age children in all countries, we used the MS criteria on adolescents defined by the American National Cholesterol Education Program-Adult Treatment Panel III (NECP-ATP III) described by Cook and others.^{15,16} The subjects who matched 3 indexes or more in the following 5 indexes were diagnosed with MS: 1) Abdominal obesity, WC \geq the 90th percentile value at the same age and sex; 2) Hypertension, SBP and (or) DBP \geq the 90th percentile value at the same age and sex; 3) Hypertriglyceridemia,

TG \geq 1.24 mmol/L; 4) HDL-C \leq 1.03 mmol/L; 5) Hyperglycemia, FPG \geq 5.6 mmol/L. WC criterion was referred to the WC percentile value established according to 160,225 Chinese children aged 7~18 years by Ji CY¹⁷ and blood pressure criterion was referred to Blood Pressure Reference of Chinese Children and Adolescents in 2005 established by Mi J.¹⁸ According to the WHO criteria, serum vitamin A concentrations lower than 0.7 µmol/L were classified as vitamin A deficiency (VAD) and values between 0.70 and 1.05 µmol/L were defined as marginal vitamin A deficiency (MVAD), and serum vitamin A concentrations higher than 1.05 µmol/L were classified

as sufficient vitamin A. Both VAD and MVAD were col-

Data management and statistical analysis

lectively referred as insufficient vitamin A.¹⁹

The data entry forms, built with range and consistency checks, were designed with Microsoft Office Excel. Statistical analysis was performed with SPSS software version 19.0. Continuous variables were presented as Mean±SD while categorical variables were presented as percentage rate. Differences in measurement data were compared with Student's *t*-test or analysis of variance (ANOVA) and the enumeration data were assessed with Pearson Chi-Square test. Multiple logistic regression models were used to calculate odds ratios (ORs) and 95% confidence intervals (CIs). All reported probabilities (*p*-values) were two sided, with p<0.05 considered as statistically significant.

Ethical considerations

All of the children were informed of the purpose of the study, and their participation in the study was voluntary. Parents gave written consent before their children were enrolled into the study. The survey was reviewed and approved by the institutional ethical committee of the Children's Hospital of Chongqing Medical University.

RESULTS

General characteristics of study population

There were 981 boys and 947 girls aged $7\sim11$ years recruited in this cross-sectional study. The participants' overweight rate was 10.1% and the obesity rate was 6.7%. Boys' overweight rate and obesity rate were 12.4% and 9.2%, respectively, while girls' overweight rate and obesity rate were 7.7% and 4.1%, respectively. Based on the test of Pearson Chi-Square, there was a significant difference between boys' and girls' overweight rates and obesity rates (p<0.001). There were 274 cases of MVAD, 53 cases of VAD, taking 14.2% and 2.8% of the investigated subjects respectively, so 327 cases of vitamin A insufficiency occurred, taking 17.0% of all investigated subjects. In our study, the occurrence of one index of metabolic disorders, two indexes of metabolic disorders and metabolic syndrome were 17.3%, 5.6% and 3.5%, respectively. (Table 1)

Vitamin A and metabolic risk indicators levels by body weight

Metabolic risk indicators, including WC, SBP, DBP, TG and FPG levels of school-age children in overweight group and obese group were significantly higher than those of children in normal weight group (p<0.05), but HDL-C levels in overweight group and obese group were significantly lower than those of children in normal weight group (p<0.05). The levels of serum vitamin A in obese group were significantly lower than those in overweight group and normal weight group (p<0.05). FPG levels between obese group and overweight group had no significant difference. Moreover, WC, SBP, DBP and TG levels gradually increased but vitamin A and HDL-C gradually decreased with the increase of BMI. (Table 2)

Comparison of metabolic risk factors according to vitamin A status

BMI, WC, HDL-C and FPG were strongly associated with vitamin A status (p<0.05). Compared with sufficient vitamin A group, the levels of BMI, WC and FPG were significantly higher in the insufficient vitamin A group (p<0.05), however, the levels of HDL-C were significantly lower in the insufficient vitamin A group (p<0.05), while the levels of SBP, DBP and TG had no significant difference between insufficient vitamin A group and sufficient vitamin A group. (Table 3)

Crude and adjusted risks of vitamin A insufficiency with metabolic factors status

Table 4 showed the crude and adjusted Odds Ratio (OR)

Table 1.	General	characteristic	s of study	population'

Items	Characteristics	n (%)
Sex	Boys	981 (50.9)
	Girls	947 (49.1)
Body weight	Normal weight	1604 (83.2)
	Overweight	195 (10.1)
	Obesity	129 (6.7)
Vitamin A	VAN	1601 (83.0)
	MVAD	274 (14.2)
	VAD	53 (2.8)
Metabolic indexes (WC, BP, TG, HDL-C, and FPG)	=0 MS component	1419 (73.6)
	=1 MS component	334 (17.3)
	=2 MS components	107 (5.6)
	MS (>3 MS components)	68 (3.5)

VAN: vitamin A normal; MVAD: marginal vitamin A deficiency; VAD: vitamin A deficiency; WC: waist circumference; BP: blood pressure; TG: triglyceride; HDL-C: high density lipoprotein cholesterol; FPG: fasting blood glucose; MS: metabolic syndrome. [†]Data are expressed as n (%). of vitamin A insufficiency with metabolic factors status. In the crude analysis, obesity, hypertriglyceridemia, hyperglycaemia and MS were found to be significantly associated with vitamin A insufficiency ($\leq 1.05 \ \mu$ mol/L) (p<0.05), but overweight, high SBP, high DBP and low HDL-C were not found to be significantly associated with vitamin A insufficiency. In the multivariate model (adjusted by age and sex), obesity, hypertriglyceridemia, hyperglycaemia and MS remained significant (p<0.05), Compared with normal children, obesity had a 2.37-fold (95% CI: 1.59, 3.55) greater risk of having vitamin A insufficiency, and MS had a 1.99-fold (95% CI: 1.14, 3.47) greater risk of having vitamin A insufficiency.

Crude and adjusted risks of metabolic syndrome with vitamin A status

Table 5 showed both the crude and adjusted Odds Ratio (OR) of MS with vitamin A status. In the crude analysis, VAD was found to be significantly associated with MS (p=0.017). In the multivariate model (adjusted by age, sex), compared with normal children, participants with VAD remained to be significantly higher risk of having MS (OR: 3.82; 95% CI: 1.44, 10.2) (p=0.007). No matter the analysis was crude or adjusted, MVAD was not found to be significantly associated with MS.

Table 2. Comparison on vitamin A and MS components in school-age children by weight status[†]

	Group				
Variable	Normal weight	Overweight	Obesity	F	<i>p</i> -value
	(n=1604)	(n=195)	(n=129)		
WC (cm)	54.9±5.41	$66.2{\pm}6.20^{\ddagger}$	73.7±9.76 ^{‡§}	865	< 0.001
SBP (mm Hg)	96.3±9.91	$103{\pm}11.2^{\ddagger}$	$113\pm12.1^{\$\$}$	174	< 0.001
DBP (mm Hg)	59.1±8.50	$63.2 \pm 9.46^{\ddagger}$	$69.5 \pm 9.30^{\$\$}$	98.0	< 0.001
TG (mmol/L)	0.70 ± 0.33	$0.92{\pm}0.48^{\ddagger}$	$1.06{\pm}0.47^{18}$	82.2	< 0.001
HDL-C (mmol/L)	1.57±0.35	$1.46\pm0.34^{\ddagger}$	$1.29{\pm}0.32^{\$\$}$	46.3	< 0.001
FPG (mmol/L)	4.82 ± 0.45	$4.91{\pm}0.49^{\ddagger}$	$4.95{\pm}0.52^{\ddagger}$	7.55	0.001
Vitamin A (µmol/L)	1.25 ± 0.25	1.23 ± 0.24	1.15±0.22 ^{‡§}	9.82	< 0.001

WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; TG: triglyceride; HDL-C: high density lipoprotein cholesterol; FPG: fasting blood glucose; MS: metabolic syndrome.

[†]ANOVA analysis and LSD test, values are mean±SD.

[‡]Compared with Normal weight group (p < 0.05).

[§]Compared with Overweight group (p < 0.05).

Table 3. Comparison of metabolic risk factors according to vitamin A status[†]

	Vitamin A in			
Metabolic risk factors	Yes (≤1.05 µmol/L)	No (>1.05 μmol/L)	t	<i>p</i> -value
	n=327	n=1601		
BMI (kg/m ²)	17.3±3.34	16.7±2.74	2.85	0.005
WC (cm)	58.6±9.74	57.0±7.69	2.74	0.007
SBP (mm Hg)	98.5±11.4	98.0±11.0	0.756	0.450
DBP (mm Hg)	60.5 ± 9.06	60.2 ± 9.08	0.555	0.579
TG (mmol/L)	0.76 ± 0.39	0.75 ± 0.38	0.576	0.565
HDL-C (mmol/L)	$1.49{\pm}0.35$	1.55±0.35	-2.94	0.003
FPG (mmol/L)	4.92 ± 0.45	4.82 ± 0.46	3.30	0.001

BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; TG: triglyceride; HDL-C: high density lipoprotein cholesterol; FPG: fasting blood glucose. [†]Student's *t* test analysis, values are expressed as mean±SD.

Table 4. Crude and adjusted risks of vitamin A insufficiency with metabolic factors status[†]

Metabolic factors	Vitamin A insufficiency			
Metabolic factors	Crude OR (95% CI)	<i>p</i> -value	Adjusted OR (95% CI)§	<i>p</i> -value
Overall overweight (BMI)	1.17 (0.80, 1.73)	0.421	1.17 (0.79, 1.74)	0.428
Overall obesity (BMI)	2.41 (1.62, 3.59)	< 0.001	2.37 (1.59, 3.55)	< 0.001
High SBP	1.17 (0.77, 1.78)	0.455	1.24 (0.81, 1.89)	0.317
High DBP	1.09 (0.65, 1.85)	0.740	1.21 (0.71, 2.06)	0.481
Hypertriglyceridemia	1.51 (1.02, 2.22)	0.038	1.64 (1.11, 2.43)	0.014
Low HDL-C	1.49 (0.98, 2.25)	0.061	1.49 (0.98, 2.26)	0.060
Hyperglycaemia	1.76 (1.09, 2.84)	0.021	1.69 (1.04, 2.75)	0.033
MS	1.81 (1.04, 3.14)	0.036	1.99 (1.14, 3.47)	0.016

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL-C: high density lipoprotein cholesterol; MS: metabolic syndrome.

^{*}Multiple logistic regression.

[§]Adjusted for age and sex.

5	6	7

Vitamin A level			MS	
	Crude OR (95% CI)	<i>p</i> -value	Adjusted OR (95% CI) [§]	<i>p</i> -value
VAD	3.23 (1.23, 8.47)	0.017	3.82 (1.44, 10.2)	0.007
MVAD	1.55 (0.83, 2.89)	0.172	1.65 (0.88, 3.09)	0.119

VAD: vitamin A deficiency; MVAD: marginal vitamin A deficiency; MS: metabolic syndrome.

[†]Multiple logistic regression.

[§]Adjusted for age and sex.

DISCUSSION

The prevalence of obesity among children has rapidly increased in the world in recent decades.²⁰⁻²² In the developed countries, taking Europe and America for example, the rate of childhood obesity had increased 3 times in the past 30 years, while in the developing country, such as Brazil, children's obesity rate rose from 4.1% in 1974 to 13.9% in 1997.^{23,24} One previous survey indicated that in the urban areas of Chongqing in 2005, the prevalence of obesity in children was about 3.7% in general, 5.0% in boys and 2.4% in girls.²⁵ In our study, the obesity in school-age children of Chongqing was 6.7% in general, 9.2% in boys, 4.1% in girls. Compared with 2005, the obesity rate of school-age children in Chongqing increased nearly twice. A large population based survey from Shanghai, the most developed metropolis in China, including 14,301 students aged 7~18 years, showed that the obese prevalence of school-age children was 7.0%.²⁶ The obesity rate of our study in Chongqing, which used the same standard, was very close to the result of Shanghai. This is a reminder to us that although the economy of Chongqing was not advanced, we should still pay more attention to obesity of school-age children.

Obesity is closely related to MS, and our study showed that MS did exist in school-age children. In 2005, International Diabetes Federation (IDF) estimated that one quarter of world population have suffered MS. Sangun Ö et al showed that the prevalence of MS among obese Turkey children was found to be 39%, 34% and 33% according to the modified WHO standard, Cook's and the IDF consensus criteria respectively.²⁷ In China, an investigation on the prevalence of MS among 20,000 students aged 6~18 years in Beijing suburbs showed that the MS rates among normal weight, overweight and obese children were 0.9%, 7.7% and 30.1%, respectively, according to Cook's criterion.²⁸ Our study showed that the prevalence of MS in normal weight, overweight and obese school-age children in Chongqing of China was 0.2%, 8.7%, and 37.2%, respectively. Our results were generally in agreement with above results and suggested that the prevalence of MS in less developed regions was comparable with those highlydeveloped regions and MS prevalence may be independently related to the economic level. In addition, our data also indicated that MS prevalence increased with the increase of BMI, which reinforces the benefit of body weight management in the prevention of MS complications.

Vitamin A is an important micronutrient for children. Our study showed that the prevalence of VAD and MVAD were 2.8% and 14.2% among the school-age children in Chongqing, respectively. Our previous study showed that the prevalence of VAD and MVAD in preschool children in the suburbs of Chongqing was 7.7% and 34.8%, respectively.²⁹ Compared with our previous study, the subjects recruited in present study were mostly living in the urban areas in Chongqing with a relatively higher quality of life, so the prevalence of VAD and MVAD in this study were lower than our previous results. However, such high prevalence of insufficient vitamin A (17.0% of the 327 subjects) was out of our expectation and suggested that vitamin A insufficiency among Chongqing urban school-age children was a severe healthy problem.

There are two possible reasons underling VAD in the human population: one is the reduced vitamin A intake and the other is the over-consumption of vitamin A. Vitamin A can only be obtained from external sources such as cod liver oil because our human body cannot produce it. Therefore, the vitamin A undersupply in the diets is the important reason causing VAD. Previously, our group investigated the preschool children from Banan District of Chongqing and found that the dietary vitamin A intake was significantly associated with the plasma retinol levels.³⁰ In this study, it is observed that the dietary patterns and habits of these children were not healthy and unbalanced nutrients intake occurred. The intake of vegetables and legumes was not sufficient, and pork was the major source of animal foods and the intake of seafood, fish and shrimps, for instance, was relatively less. These may be the direct and critical reasons contributing to nutrients insufficiency, including vitamin A insufficiency. Even though unbalanced nutrients intake is the dominant and direct factor for VAD, over-consumption of vitamin A, such as acute infection, should not be excluded. Therefore, when we recruited subjects, we had carefully excluded children who suffered from acute infection diseases, including pneumonia, upper respiratory infection and influenza, from our study. The effect of the acute infection on VAD can be eliminated in our study. In summary, we infer that the unbalanced diets may be the main factor causing VAD.

Vitamin A may play an important role in regulating body weight through the action of vitamin A metabolites. It was reported that vitamin A deficiency, as measured by low vitamin A concentrations in blood, was significantly associated with insulin resistance among adult human with obesity.^{10,31} In our study, we investigated the correlations between serum vitamin A and obesity, and found out that obesity was strongly associated with vitamin A insufficiency in school-age children: obese individuals were found to have lower vitamin A levels compared with normal weight individuals. Moreover the prevalence of obesity and vitamin A levels in school-age children appeared in an obvious negative correlation. The risks of insufficient vitamin A in obese children were 2.37 times more than those of normal children. This finding was generally agreed with previous study mentioned above. The reason may be that obese children do not take in enough vitamin A due to unbalanced diets. Meanwhile, it could also be that obese children have mal-absorption of vitamin A, further causing low concentrations of vitamin A in the obese children. It was recognized recently that vitamin A has important regulatory functions on the chronic inflammatory response. VAD increases a Thelper type 1 (Th1) response, elevates levels of proinflammatory cytokines, and increases the expression of leptin.³² Animal studies have shown that retinoic acid (RA) reduces body weight, and vitamin A-deficient diet feeding led to a marked increase of adiposity and a small increase of body weight.³³ Similarly, feeding of high doses of vitamin A results in significant reduction in body weight gain, and retroperitoneal white adipose tissue weight in obese rats.³⁴ Taken all the studies of human investigation and animal experiment, vitamin A was significantly relevant with development of obesity, and our current results further reinforced these reports.

MS consists of a cluster of metabolic conditions, such as hypertriglyceridemia, high LDL-C, low HDL-C, insulin resistance, abnormal glucose tolerance, hypertension and etc. MS among young population did exist even though no obvious clinic signs and symptoms were observed, especially in children, and the potential health threat was largely neglected. Metabolic dysfunctions formed in childhood have been recognized as the important predictor of cardiovascular diseases and type 2 diabetes in adult. It has been found that the plasma vitamin A levels were significantly lower in MS patients than those in healthy individuals.³⁵ Similar to the existing evidence, our findings showed significant associations between the vitamin A status and individual metabolic risk factors, including hypertriglyceridemia and hyperglycaemia. After adjustment by age and sex, comparing with normal children, participants with MS had significantly higher risk of having vitamin A insufficiency, at the same time, participants with VAD had significantly higher risk of having MS. But participants with MVAD had not significantly higher risk of having MS, suggesting the degree of vitamin A insufficiency may significantly affect the metabolic outcomes.

Overall, serum vitamin A is associated with obesity and MS of school-age children, but how obesity and MS lead to vitamin A insufficiency still need further investigation and study. The further study of vitamin A and MS correlation will provide new strategy and solution to prevent and intervene in metabolic diseases. Our findings have given rise to concerns about which vitamin A plays a very significant role in children health. Continuous and efficient efforts should be taken to promote the nutrition and health knowledge to both children and their parents, and also monitor and estimate vitamin A status of schoolage children. Health knowledge on the importance of vitamin A, and ways of achieving sufficient vitamin A status should also be disseminated to the public.

There are some limitations in current study. Firstly, considering the academic pressure of students of Grade Six, we only chose the students from Grade One to Grade

Five as the test subjects after discussion with relevant headmaster. Secondly, the participants of the study were all from the central downtown of Chongqing, future studies will be extended to suburbs of Chongqing and other western cities of China.

ACKNOWLEDGMENTS

We are grateful to all the staff in this study for their teamwork and persistent efforts and thankful for the school children and teachers in the primary schools in Yuzhong District of Chongqing for their participation and cooperation. Our gratitude also goes to Children's Nutrition Research Center, Children's Hospital of Chongqing Medical University for providing equipment and reagent.

AUTHOR DISCLOSURES

The authors declare that there are no conflicts of interest. This work was supported by the Natural Science Foundation Project of Chongqing (CSTC, 2010BB5370), the project of Health Bureau of Chongqing (NO. 2009-1-39 and NO. 2009-2-257).

REFERENCES

- WHO. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000;894:i-xii, 1-253. doi: 10.1017/S002193 2003245508.
- Després JP, Lemieux I. Abdominal obesity and metabolic syndrome. Nature. 2006;444:881-7. doi: 10.1038/nature054 88.
- Grundy SM. Metabolic syndrome pandemic. Arterioscler Thromb Vasc Biol. 2008;28:629-36. doi: 10.1161/ATVBA HA.107.151092.
- Druet C, Ong K, Levy Marchal C. Metabolic syndrome in children: comparison of the International Diabetes Federation 2007 Consensus with an Adapted National Cholesterol Education Program Definition in 300 Overweight and Obese French Children. Horm Res Paediatr. 2010;73:181-6. doi: 10.1159/000284359.
- Pourshahidi LK. Vitamin D and obesity: current perspectives and future directions. Proc Nutr Soc. 2015;74: 115-24. doi: 10.1017/S0029665114001578.
- Kostecka M. Eating habits of preschool children and the risk of obesity, insulin resistance and metabolic syndrome in adults. Pak J Med Sci. 2014;30:1299-303. doi: 10.12669/ pjms.306.5792.
- Rivera JA, Hotz C, González-Cossío T, Neufeld L, García-Guerra A. The effect of micronutrient deficiencies on child growth: a review of results from community-based supplementation trials. J Nutr. 2003;133:4010S-20S.
- Lin LM, Liu YL, Ma GF, Tan ZW, Zhang XL, Jiang JX, Song XF, Wang L, Zhang JN, Wang HR, Li M. Survey on vitamin A deficiency in children under-6-years in China. Chinese Journal of Preventive Medicine. 2002;36:315-9. doi: 10.3760/j:issn:0253-9624.2002.05.008. (In Chinese)
- Villaca Chaves G, Pereira SE, Saboya CJ, Ramalho A. Nonalcoholic fatty liver disease and its relationship with the nutritional status of vitamin A in individuals with class III obesity. Obes Surg. 2008;18:378-85. doi: 10.1007/s11695-0 07-9361-2.
- 10. Viroonudomphol D, Pongpaew P, Tungtrongchitr R, Changbumrung S, Tungtrongchitr A, Phonrat B, Vudhivai N, Schelp FP. The relationships between anthropometric measurements, serum vitamin A and E concentrations and lipid profiles in overweight and obese subjects. Asia Pac J Clin Nutr. 2003;12:73-9.
- 11. Yu DM, Zhao LY, Piao JH, Zhang J, Hu XQ, Fu P. Prevalence of the metabolic syndrome and its main

influencing factors in 7-17 years old children and adolescents in 8 provinces. Chinese Journal of Health Educaton. 2012,28:431-7. (In Chinese)

- Valler-Jones T, Wedgbury K. Measuring blood pressure using the mercury sphygmomanometer. Br J Nurs. 2005;14: 145-50. doi: 10.12968/bjon.2005.14.3.17519.
- Hariharan M, VanNoord T, Greden JF. A high-performance liquid-chromatographic method for routine simultaneous determination of nicotine and cotinine in plasma. Clin Chem. 1988;34:724-9.
- 14. Group of China Obesity Task Force. Body mass index reference norm for screening overweight and obesity in Chinese children and adolescents. Chinese Journal of Epidemiology. 2004;25:97-102. doi: 10.3760/j.issn:0254-64 50.2004.02.003. (In Chinese)
- 15. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994. Arch Pediatr Adolesc Med. 2003;157:821-7. doi: 10.1001/archpedi.157.8. 821.
- 16. Zimmet P, Alberti G, Kaufman F, Tajima N, Silink M, Arslanian S, Wong G, Bennett P, Shaw J, Caprio S, International Diabetes Federation Task Force on Epidemiology and Prevention of Diabetes. The metabolic syndrome in children and adolescents. Lancet. 2007;369: 2059-61.
- 17. Ji CY, Yt Sung R, Ma GS, Ma J, He ZH, Chen TJ. Waist circumference distribution of Chinese school-age children and adolescents. Biomed Environ Sci. 2010;23:12-20. doi: 10.1016/S0895- 3988(10)60026-8.
- Mi J, Wang TY, Meng LH, Zhu GJ, Han SM, Zhong Y. Development of blood pressure reference standards for Chinese children and adolescents. Chinese Journal of Evidence-Based Pediatrics. 2010;5:4-14. doi: 10.3969/j.issn. 1673-5501.2010.01.002. (In Chinese)
- WHO. Indicators for Assessing Vitamin A Deficiency and Their Application in Monitoring and Evaluating Intervention Programmes. Geneva: World Health Organization; 1996.
- Han JC, Lawlor DA, Kimm SY. Childhood obesity. Lancet. 2010;375:1737-48. doi: 10.1016/S0140-6736(10)60171-7.
- Hills AP, Mokhtar N, Brownie S, Byrne NM. Childhood obesity in Asia: the value of accurate body composition methodology. Asia Pac J Clin Nutr. 2014;23:339-43. doi: 10. 6133/apjcn.2014.23.3.07.
- 22. Rivera JÁ, de Cossío TG, Pedraza LS, Aburto TC, Sánchez TG, Martorell R. Childhood and adolescent overweight and obesity in Latin America: a systematic review. Lancet Diabetes Endocrinol. 2014;2:321-32. doi: 10.1016/S2213-85 87(13)70173-6.
- Ogden CL, Carroll MD, Curtin LR, Lamb MM, Flegal KM. Prevalence of high body mass index in US children and adolescents, 2007-2008. JAMA. 2010;303:242-9. doi: 10. 1001/jama.2009.2012.

- 24. Gupta N, Goel K, Shah P, Misra A. Childhood obesity in developing countries: epidemiology, determinants, and prevention. Endocr Rev. 2012;33:48-70. doi:10.1210/er.201 0-0028.
- 25. Xiong F, Zeng Y, Long CL, Wang DG, Zhu M, Luo YH. Epidemiological survey of obesity and its related diseases in children and adolescents aged 3 to 18 years in Chongqing urban areas. Chongqing Medicine. 2005;34:1838-40. doi: 10. 3969/j.issn.1671-8348.2005.12.033. (In Chinese)
- 26. Yang Y, Chen PJ, Wu YQ, Peng NN, Zhou GY. Study on risk factors of overweight and obesity school-age children and adolescents in Shanghai. Chinese Journal of School Health. 2012;33:1350-55. (In Chinese)
- 27. Sangun Ö, Dündar B, Köşker M, Pirgon Ö, Dündar N. Prevalence of metabolic syndrome in obese children and adolescents using three different criteria and evaluation of risk factors. J Clin Res Pediatr Endocrinol. 2011;3:70-6. doi: 10.4274/jcrpe.v3i2.15.
- Wan NJ, Mi J, Wang TY, Duan JL, Li M, Gong CX, Du JB, Zhao XY, Cheng H, Hou DQ, Wang L. Metabolic syndrome in overweight and obese schoolchildren in Beijing. Chinese Journal of Pediatrics. 2007;45:417-21. doi: 10.3760/j.issn: 0578-1310.2007.06.005. (In Chinese)
- 29. Li TY, Qu P, Wang R, Lian XM, Mao CT, Dai Y. Effect of vitamin A-fortified biscuits on preschool children in Chongqing, China. Sight and Life Newsletter. 2003;2:45-8.
- 30. Peng P, Wei X, Liang X, Chen J, Liu Y, Zhang T, Li T. Effect of dietary vitamin A intake on plasma vitamin A concentration in preschool children of Banan district, Chongqing, China. Journal of Peking University (Health Sciences). 2014;46: 366-72. doi: 10.3969/j.issn.1671-167X.2014.03.006. (In Chinese)
- 31. Strauss RS. Comparison of serum concentrations of alphatocopherol and beta-carotene in a cross-sectional sample of obese and nonobese children (NHANES III). National Health and Nutrition Examination Survey. J Pediatr. 1999; 134:160-5. doi: 10.1016/S0022-3476(99)70409-9.
- García OP. Effect of vitamin A deficiency on the immune response in obesity. Proc Nutr Soc. 2012;71:290-7. doi: 10. 1017/S0029665112000079.
- 33. Ribot J, Felipe F, Bonet ML, Palou A. Changes of adiposity in response to vitamin A status correlate with changes of PPAR gamma 2 expression. Obes Res. 2001;9:500-9. doi: 10.1038/oby.2001.65.
- 34. Jeyakumar SM, Vajreswari A, Giridharan NV. Vitamin A regulates obesity in WNIN/Ob obese rat; independent of stearoyl-CoA desaturase-1. Biochem Biophys Res Commun. 2008;370:243-7. doi: 10.1016/j.bbrc.2008.03.073.
- 35. Godala M, Materek-Kuśmierkiewicz I, Moczulski D, Rutkowski M, Szatko F, Gaszyńska E, Kowalski J. Estimation of plasma vitamin A, C and E levels in patients with metabolic syndrome. Pol Merkur Lekarski. 2014;36: 320-3.

Original Article

Serum vitamin A status is associated with obesity and the metabolic syndrome among school-age children in Chongqing, China

Xiaoping Wei MD^{1,2,3,4}, Rong Peng MD^{1,4}, Jiaoyang Cao MD^{1,4}, Yu Kang PhD^{2,3,4}, Ping Qu MD^{2,3,4}, Youxue Liu PhD^{1,2,3,4}, Xiaoqiu Xiao PhD^{2,3,4}, Tingyu Li MD^{1,2,3,4}

¹Children's Nutrition Research Center, Children's Hospital of Chongqing Medical University, Chongqing, PR China

²Ministry of Education Key Laboratory of Child Development and Disorders, Children's Hospital of Chongqing Medical University, Chongqing, PR China

³Chongqing International Science and Technology Cooperation Center for Child Development and Disorders, Children's Hospital of Chongqing Medical University, Chongqing, PR China

⁴Key Laboratory of Paediatrics in Chongqing, Children's Hospital of Chongqing Medical University, Chongqing, PR China

中国重庆地区学龄期儿童血清维生素 A 营养状况与肥 胖和代谢综合征的关系

本研究旨在观察中国重庆地区学龄期儿童维生素 A 营养状况与肥胖和代谢综合征的关系。横断面调查重庆市渝中区 5 所小学共 1,928 名学龄期儿童。检查 其身高、体重、腰围和血压水平,检测其血清维生素 A、血糖和血脂水平。结 果显示,调查对象的超重率为 10.1%,肥胖率为 6.7%;代谢综合征发生率为 3.5%;维生素 A 缺乏(VAD)发生率为 2.8%,边缘型维生素 A 缺乏 (MVAD)发生率为 14.2%。肥胖组儿童血清维生素 A 水平显著低于超重组 和正常组。体质指数、腰围、高密度脂蛋白胆固醇和血糖水平与维生素 A 营 养状况有关 (p < 0.05)。校正年龄和性别后,肥胖儿童发生维生素 A 不足 ($\leq 1.05 \mu mol/L$)的风险是正常儿童的 2.37 倍 (95% CI: 1.59, 3.55), (p < 0.001),代谢综合征儿童发生维生素 A 不足的风险是正常儿童的 1.99 倍 (95% CI: 1.14, 3.47, p = 0.016),同时我们发现,VAD 的儿童发生代谢综 合征的风险是正常儿童的 3.82 倍 (95% CI: 1.44, 10.2, p = 0.007)。重庆市 城区学龄期儿童 VA 不足的发生率较高,是一个较严重的健康问题,维生素 A 不足与肥胖和代谢综合征有关。

关键词:维生素 A、代谢综合征、肥胖、学龄期儿童、体质指数