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Prevalence and associated factors of impaired renal function in Chinese children: the China Health and Nutrition Survey

Peige Song^{1,2}, Manli Wang¹, Xinlei Chang¹, Jiawen Wang³, Wei Wei³, and Lin An^{1,*}

¹Department of Maternal and Child Health, School of Public Health, Peking University, Beijing 100191, China

²Centre for Population Health Sciences, University of Edinburgh, Edinburgh EH8 9AG, UK

³Institute of Medical Humanities, Peking University, Beijing 100191, China

Abstract

Aim—To assess the prevalence of impaired renal function and its associated factors in Chinese children.

Methods—Children aged 7–18 years in China Health and Nutrition Survey (CHNS) 2009 were included as participants, and their anthropometric measurements, blood pressure (BP) and biochemical parameters were taken for analysis. The estimated glomerular filtration rate (eGFR) was calculated by using the Schwartz “original” formula.

Results—The prevalence of estimated glomerular filtration rate (eGFR) < 90 ml/min/1.73 m² and < 75 ml/min/1.73 m² was 10.09% (95% CI: 8.03–12.11) and 1.01% (95% CI: 0.38–1.77) respectively. The prevalence of impaired renal function (eGFR < 60 ml/min/1.73 m²) was 0.25%. Age was detected as a negative associated factor whereas hyperuricemia and elevated total cholesterol (TC) were positively associated factors for subjects with eGFR < 90 ml/min/1.73 m². In the group of eGFR < 75 ml/min/1.73 m², only elevated TC was related to the increased odds of decreased eGFR.

Conclusions—Our findings underscore the need for large-scale programs to detect and treat the early-stage impaired renal function in the paediatric population in China.

Keywords

prevalence; impaired renal function; children; China

Background

Chronic kidney disease (CKD), which is a set of conditions characterised by declined kidney function that may progress to end-stage renal disease (ESRD)^{1,2}, has become a serious public health problem in the past decades globally^{3–5}. The burden of CKD is not only

*Correspondence: Lin An, Department of Maternal and Child Health, School of Public Health, Peking University, Beijing 100191, China (anlinbjmu@163.com; Tel: +86-10-8280-1222).

Conflict of interests

All the authors declare that they have no competing interests about this article.

limited to its implications on demands for dialysis or kidney transplantation in the final stage, but also includes adverse impacts on the patients' health and quality of life^{6,7}. The association between the increased cardiovascular risks and ESRD has been established, where the cardiovascular mortality rates are ten to one hundred folds higher in dialysis patients than the general population^{8,9}.

Along with the epidemic of cardiovascular risk factors in the 21st century, it is estimated that around 8–16% of the population worldwide are affected by CKD, with substantial morbidity and mortality as well as high economic burden². Moreover, the situation is still getting worse with the number of CKD patients rising markedly, especially in adults^{1,10}.

According to the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-KDOQI), CKD is defined as a presence of abnormalities of kidney structure or function (for example, pathological, laboratory or imaging findings) for 3 months or an estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m² for 3 months, and can be classified into 5 stages of severity, with the stage 1 as mild disease and the stage 5 as ESRD¹. This classification is also applicable for children aged more than 2 years¹¹.

In epidemiologic studies, the presence of CKD is commonly assessed by eGFR and albuminuria^{12,13}. Since the release of the KDOQI guidelines in 2003¹⁴, a number of population-based epidemiologic studies adopting this classification system have been conducted in both developed and developing countries^{12,15}. For the largest developing country China, a national investigation has revealed a lower prevalence of CKD in adults (10.8%) than those in western countries, such as the US and Canada, where the prevalence of CKD was estimated to be as high as 15.5%¹⁶. However, given the large size of more than 100 million CKD patients across the whole country who may need intensive health care in the future, special attention is still needed to better detect CKD in the early stage in China.

Understanding the epidemiology of CKD in children is a crucial first step to slow or prevent progression into ESRD in the later life¹⁷. Globally, most of the epidemiologic studies of CKD were conducted in adults, the prevalence and incidence of CKD in younger population are still largely understudied^{1,17,18}. This is also the case for China, where the prevalence of CKD in Chinese children is still unknown. In this cross-sectional study, we used the data from the China Health and Nutrition Survey (CHNS) in 2009¹⁹, a national population-based study, to assess the prevalence of impaired renal function in Chinese children and to evaluate possible associated factors of decreased eGFR.

Methods

Study population and data collection

As a national household-based cross-sectional study, CHNS has been conducted successively in nine provinces (Shandong, Liaoning, Jiangsu, Hunan, Hubei, Henan, Heilongjiang, Guizhou, and Guangxi) for nine times (in 1989, 1991, 1993, 1997, 2000, 2004, 2006, 2009 and 2011)^{20,21}. The detailed study design and methods have been published elsewhere²¹. In brief, survey sites with different geographies, economic development levels, and health indicators were drawn by a multistage random cluster

sampling process in each province²¹. The questionnaire information includes basic socioeconomic factors and health, nutritional, and demographic measures. Fasting blood samples were only collected in 2009 from individuals equal or older than 7 years^{21,22}. For the purpose of our study, only the data of CHNS 2009 were adopted because of the availability of biochemical data. All children and their parents provided written informed consent, and the study protocols were approved by the Institutional Review Boards of the University of North Carolina, Chapel Hill and the Chinese Centre for Disease Control²¹.

Sample size

The required sample size was calculated for the primary objective taking the prevalence of children with eGFR < 90 ml/min/1.73 m² to be estimated at 3.5%¹⁸. The sample size should be at least 325 with 95% confidence level and 2% bound on estimation error. In this study, a total of 793 children were included.

Measurements

Anthropometric measurements were taken by well-trained observers according to standard procedures. Weight was measured with lightweight clothing using a calibrated beam scale, height was measured without shoes using a portable stadiometer, and waist circumference (WC) was measured at the midpoint between the lowest rib and the iliac crest in a horizontal plane using a non-elastic tape. Weight was accurate to 0.1 kg, height and WC were both to 0.1 cm. Body mass index (BMI) was then calculated as weight (in kg) divided by the square of height (in m).

According to the standard protocol, blood pressure (BP) was measured three times by trained nurses and physicians by mercury sphygmomanometers. An appropriate size of cuff was chosen to fit the children's arm circumference, Korotkoff phase 1 and Korotkoff phase 5 were used for defining systolic blood pressure (SBP) and diastolic blood pressure (DBP)²³. The measurements were collected after a 10-minutes seated rest and the average value of the three measurements was used for analysis^{24,25}.

Fasting blood samples were taken from participants aged 7 years and above by trained nurses and physicians. Glucose and haemoglobin A1c were tested immediately in survey sites. The serum and plasma samples were refrigerated at -86°C, and then shipped to a national central lab in Beijing, where all specimens were analysed with stringent quality control. Haemoglobin (Hb) was analysed using the volume, conductivity, light scatter method, high-density lipoprotein cholesterol (HDL) and low-density lipoprotein cholesterol (LDL) using the enzymatic method, total cholesterol (TC) using the cholesterol oxidase—phenol and aminophenazone method, triglyceride (TG) using the glycerol-3-phosphate oxidase—phenol and aminophenazone method, serum creatinine (Scr) using the picric acid method, and serum uric acid (UA) using the enzymatic colorimetric method.

Definitions

Cities, suburban areas, towns and county capital cities were classified as the urban area and villages as the rural area.

To better control the variance of race/ethnicity, BMI was categorized according to the Chinese gender-and age- specific classification²⁶. a BMI < the 5th percentile for age and gender was defined as an underweight status, a BMI < the age- and gender- specific 95th and 85th percentiles as an overweight status, and a BMI the age- and gender- specific 95th percentile as an obesity status. Abdominal obesity was also defined according to the Chinese classification as a WC 90th percentile for gender and age²⁰.

According to definitions in the “Fourth Report on Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents”, prehypertension referred to an SBP and/or a DBP 90th percentile and < 95th percentile for gender, age, and height, and hypertension referred to an SBP and/or a DBP 95th percentile for gender, age, and height^{24,27}.

In accordance with World Health Organization criteria, a Hb < 130g/l for boys aged 15 years, < 120g/l for girls aged 15 years, < 120g/l for children aged 12 and < 15 years, and < 115g/l for children aged 5 and < 12 years was defined as anaemia²⁸.

Because no universally accepted definition of hyperuricemia exists in the paediatric population, in this study, hyperuricemia was defined using three thresholds of a UA value > 327µmol/l, 357µmol/l, and > 416µmol/l respectively²⁹.

Dyslipidemia was defined as at least one abnormal value for TC, HDL, LDL or TG: elevated TC was defined as a TC > 5.1mmol/l, low HDL as an HDL < 0.9mmol/l, elevated LDL as an LDL > 3.4mmol/l, and elevated TG as a TG > 1.7mmol/l³⁰.

eGFR was calculated by using the Schwartz “original” formula because Scr was measured by using the picric acid method (Jaffe method)³¹, where $eGFR = k * height(cm) / Scr(mg/dl)$, and k was 0.70 if boys 13 years, and 0.55 otherwise. According to the KDOQI definition of CKD, the presence of decreased eGFR should last for at least 3 months¹, as a result, we were not able to identify children with CKD based on one time eGFR only. In this study, eGFR below 60 ml/min/1.73 m² were defined as impaired renal function rather than CKD. In addition, two cut-off points (90 ml/min/1.73 m² and 75 ml/min/1.73 m²) of decreased eGFR were chosen to compare our data with the results in the population-based survey of Chronic RENal Disease In Turkey (CREDIT study)¹⁸.

Statistical analysis

Continuous data were expressed as means (±SD) while categorical data as percentages. Comparisons of continuous data and categorical data were carried out using t-test and χ^2 -test respectively. The age- and gender-specific prevalence of decreased eGFR and impaired renal function was assessed. We used logistic regression models to explore the association between potential associated factors and the presence of decreased eGFR, the association was assessed by the forward selection (likelihood ratio) method. We reported both univariable and multivariable adjusted odds ratios (ORs), with 95% confidence intervals (CIs). A two-tailed P value < 0.05 was deemed as statistically significant. All analyses were carried out using SPSS 22.0 (IBM Corporation, Armonk, New York, USA).

Results

A total of 793 children aged 7–18 years participated in this survey, among them, 431 (54.35%) were boys and 362 (45.65%) were girls. The basic demographic and clinical characteristics of the study subjects are presented in Table 1. The mean age of the subjects was 12.21 ± 2.99 years for boys and 12.30 ± 2.90 years for girls. Boys had higher WC, Hb, UA, Scr and eGFR than girls, whereas girls showed higher levels of lipid profile (TC) than boys.

Only two children were assessed with impaired renal function ($\text{eGFR} < 60 \text{ ml/min/1.73 m}^2$) in the survey, which yielded an overall prevalence of 0.25%. The prevalence of $\text{eGFR} < 90 \text{ mL/min/1.73 m}^2$ and $< 75 \text{ ml/min/1.73 m}^2$ was all slightly higher in boys than girls (10.21% vs. 9.94% and 1.16% vs. 0.83% respectively). The comparison of the prevalence of decreased eGFR and impaired renal function in Chinese and Turkey children is presented in Figure 1, the estimates of eGFR in these two populations were both based on the Schwartz “original” formula. Overall, Chinese children had a much higher prevalence of $\text{eGFR} < 90 \text{ ml/min/1.73 m}^2$ than the Turkish children (10.09% vs. 3.47%). The prevalence of childhood decreased eGFR ($< 75 \text{ ml/min/1.73 m}^2$) was slightly higher in Chinese children than in Turkish children (1.01% vs. 0.94%)

As shown in Table 2, subjects in the $\text{eGFR} < 90 \text{ ml/min/1.73 m}^2$ group had significantly younger age, lower value of weight, height, WC and eGFR, and higher value of UA, TC, TG, Scr than subjects with $\text{eGFR} \geq 90 \text{ ml/min/1.73 m}^2$. Similarly, it is indicated that subjects with $\text{eGFR} < 75 \text{ ml/min/1.73 m}^2$ had lower weight, WC, eGFR, and higher UA, TC, LDL and Scr values than subjects with $\text{eGFR} \geq 75 \text{ ml/min/1.73 m}^2$.

From the results of univariable logistic regression models (Table 3), for subjects with $\text{eGFR} < 90 \text{ ml/min/1.73 m}^2$, negative correlation between age and decreased eGFR was revealed, with an OR of 0.91 (95% CI: 0.84–0.98). Hyperuricemia (UA $\geq 357 \mu\text{mol/l}$), elevated TC, elevated LDL and dyslipidemia were all potential risk factors. After adjustment for all other variables, negative correlation between age and decreased eGFR still existed (OR: 0.89 (95% CI: 0.82–0.97)) whereas the potential risk factors were only hyperuricemia (UA $\geq 357 \mu\text{mol/l}$) and elevated TC. To avoid overfitting model, in the decreased eGFR group of $< 75 \text{ ml/min/1.73 m}^2$, only univariable logistic regression analysis was conducted, elevated TC, elevated LDL and dyslipidemia were all found to be potential risk factors.

Discussion

Literature data on the prevalence of CKD in the younger population are scanty¹. This is the second population-based study worldwide reporting the prevalence and associated factors of childhood impaired renal function at the national level. For the first time, the prevalence of impaired renal function in general Chinese children was revealed as 0.25% in our study, and the prevalence of $\text{eGFR} < 90$ and $< 75 \text{ ml/min/1.73 m}^2$ was found to be 10.09% and 1.01% respectively. Moreover, age and decreased eGFR were negatively related, indicating age's protective effect on the renal function. Hyperuricemia (threshold of UA $\geq 357 \mu\text{mol/l}$) was assessed as a positively associated factor of the presence of $\text{eGFR} < 90 \text{ ml/min/1.73 m}^2$

but not for eGFR of <75 ml/min/1.73 m². The association between elevated TC and decreased eGFR was persistently strong, especially in the lower eGFR children.

The most significant merit of this survey is a large-scale, nation-wide sample of Chinese children, the adoption of standardised protocols, strict investigation procedures, and strict quality control. In addition, measurement bias can be largely avoided because all the analyses of specimens were conducted in a central laboratory in Beijing.

Scr is routinely used as a surrogate to evaluate renal function, in laboratory assessment, Scr values are mainly determined by the assay method, and the bias in Scr assessments has been a concern when classifying the renal function based on the Scr values. For example, at low levels of Scr, the enzymatic creatinine assays were turned out to be more specific than the Jaffe method³¹. In the estimation of eGFR, it is essential to choose the right equation based on the assay method. Although efforts have been made to advocate the standardisation of the reference method based on isotope dilution-mass spectrometry globally³², the Jaffe method remains the most commonly used method due to its simplicity and low cost, especially in large population studies³³. In this study, the Jaffe method using picric acid was adopted. According to the KDOQI for CKD in children and adolescents, the normal GFR values should be from 126 to 140 ml/min/1.73 m² in children aged from 2 to 20 years³⁴. Our participants showed relatively lower values of eGFR in both boys and girls (109.36±16.88 ml/min/1.73 m² and 105.38±12.89 ml/min/1.73 m²), there are three potential reasons: firstly, the subjects in our analysis were children aged from 7-18 years, negative correlation between age and decreased eGFR was previously detected, the elevated average age may cause lower average eGFR values; Secondly, the Jaffe method, where Scr is measured by a colorimetric reaction with picric acid, may bring overestimation of Scr and thus underestimation of eGFR³¹; Thirdly, ethnicity difference may play a role, it has been proven that normal GFR values are lower in Asian adults than in Caucasians adults³⁵, our study shed a light on an additional racial difference in the paediatric population.

The prevalence of childhood CKD and decreased eGFR has been previously reported in Turkish children, our results are in line with their findings, the same Jaffe assay methods and adoption of KDOQI classification guaranteed the comparability. The prevalence of eGFR <90 ml/min/1.73 m² in Chinese children was significantly different from Turkish children, multiple factors may contribute to the comparatively high prevalence of decreased eGFR of <90 ml/min/1.73 m² in Chinese children, such as the difference of age structure, and the difference of ethnicity. However, the prevalence of eGFR <75 ml/min/1.73 m² was in consistency in these two different populations. Nevertheless, the comparability of CKD prevalence is limited because few impaired renal function children were detected in our survey. Although the prevalence of impaired renal function was found not prevalent in Chinese children, by extrapolating our findings, the number of children aged 7-18 years with impaired renal function in China might be as high as 0.49 million. Given their potential progress into kidney failure and ESRD, it is crucial for the policy makers and caregivers to realize this potential upcoming challenge.

Another aim of this study was to identify associated factors for childhood impaired renal function. Although this cross-sectional survey design cannot examine causal relationship

between various associated factors and impaired renal function, we included the most common associated factors in paediatric populations to identify the potential risks of general obesity, abdominal obesity, anaemia, hypertension, hyperuricemia, low HDL, elevated LDL, elevated TC, elevated TG and dyslipidemia. This is the most in-depth attention in exploring the associated factors for childhood CKD at the population level. However, in this study, we were unfortunately not able to conduct multivariable logistic regression because the small sample size of impaired renal function and decreased eGFR group of $< 75 \text{ ml/min/1.73 m}^2$ may result in low statistical power. Although evidence from previous studies suggested a high prevalence of CKD in elderly adults³⁶, the association of renal functional decline with age is not universal³⁷. Both our study and the CREDIT study revealed a negative relationship between increased age and decreased eGFR prevalence in children, this may be related to the biological features of growth but cannot suggest a certainly decreased prevalence of CKD in older children. Among all the metabolic factors, elevated TC turned out to be the one with the greatest impact on decreased eGFR, which is also in accordance with the Turkish study and other previous studies^{18,38}. Furthermore, as a direct consequence of a decreased kidney function, hyperuricemia was only observed to be positively associated with decreased eGFR in the eGFR $< 90 \text{ ml/min/1.73 m}^2$ group, further studies are still needed to verify the effects.

It is still worth pointing out the limitations. Firstly, GFR was estimated by using equations other than direct measurement, this approach may over- or underestimate the actual GFR in Chinese children because the Schwartz formula was developed in American children³¹. Furthermore, in the survey, no imaging or urinary albumin assessment was conducted, children with albuminuria or microalbuminuria were not included in our estimation of impaired renal function prevalence, because of the lack of urinalysis in the investigation, this may result in underestimation of our prevalence of impaired renal function. Considering all the potential bias mentioned above, it is difficult to conclude whether the reported prevalence was underestimated or overestimated, further studies are needed to reveal the actual impaired renal function and CKD prevalence in Chinese children.

In conclusion, our study revealed the prevalence of impaired renal function in Chinese children for the first time, and validated the findings in Turkish children. Our findings underscore the need to advocate the isotope dilution-mass spectrometry method for measurements of Scr and establish large-scale programs to detect and treat the early-stage impaired renal function and CKD in the paediatric population in China. Further longitudinal studies are needed to better understand the associated risk factors of impaired renal function and CKD in children.

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Figure 1.

Comparison of the prevalence of children with decreased eGFR and impaired renal function in China and Turkey.

Table 1

Basic characteristics of the study subjects with respect to gender.

Characteristic	Total (n=793)	Boys (n=431)	Girls (n=362)
Age (years)	12.25±2.94	12.21±2.99	12.30±2.90
Residence			
Urban (%)	337 (42.50)	172 (39.91)	165 (45.58)
Rural (%)	456 (57.50)	259 (60.09)	197 (54.42)
Weight (kg)	39.64±13.14	40.30±13.95	38.86±12.08
Height (cm)	147.30±15.85	148.24±17.05	146.19±14.24
BMI (kg/m ²)	17.77±3.33	17.80±3.38	17.72±3.26
WC (cm)	63.26±9.62	64.08±10.18	62.27±8.82 *
SBP (mmHg)	100.05±13.03	100.51±13.41	99.51±12.56
DBP (mmHg)	66.67±9.51	66.80±9.50	66.52±9.54
Hb (g/l)	137.64±16.24	140.46±16.25	134.29±15.61 *
UA (μmol/l)	310.06±85.16	328.74±90.09	287.81±73.02 *
TC (mmol/l)	3.88±0.70	3.81±0.70	3.96±0.69 *
HDL (mmol/l)	1.44±0.54	1.42±0.35	1.46±0.70
LDL (mmol/l)	2.20±0.89	2.18±1.07	2.23±0.62
TG (mmol/l)	1.00±0.70	0.98±0.75	1.03±0.62
Scr (mg/dl)	0.81±0.15	0.84±0.16	0.77±0.11 *
eGFR (ml/min/1.73 m ²)	107.55±15.31	109.36±16.88	105.38±12.89 *

Data are means ± SD or n (%);

* Significantly different from boys (P<0.05).

Table 2

Basic characteristics of the study subjects respect to eGFR.

Characteristic	eGFR < 90 ml/min/1.73 m ² (n=80)	eGFR 90 ml/min/1.73 m ² (n=713)	eGFR < 75 ml/min/1.73 m ² (n=8)	eGFR 75 ml/min/1.73 m ² (n=785)	Total (n=793)
Age (years)	11.53±3.17 [*]	12.33±2.91	10.30±2.06	12.27±2.95	12.35±3.06
Gender					
Boys (%)	44(55.00)	387 (54.28)	5(62.50)	426 (54.27)	431 (54.35)
Girls (%)	36(45.00)	326 (45.72)	3(37.50)	359 (45.73)	362 (45.65)
Residence					
Urban (%)	32(40.00)	305 (42.78)	4(50.00)	333 (42.42)	337 (42.50)
Rural (%)	48(60.00)	408 (57.22)	4(50.00)	452 (57.58)	456 (57.50)
Weight (kg)	33.69±11.99 [*]	40.31±13.10	30.08±9.44 [†]	39.74±13.14	39.64±13.14
Height (cm)	137.51±15.30 [*]	148.40±15.54	136.58±16.84	147.41±15.82	147.30±15.85
BMI (kg/m ²)	17.20±3.19	17.83±3.34	15.76±1.97	17.79±3.33	17.77±3.33
WC (cm)	58.81±9.40 [*]	63.76±9.52	55.79±8.16 [†]	63.33±9.61	63.26±9.62
SBP (mmHg)	97.56±10.84	100.33±13.23	92.78±7.96	100.11±13.05	100.05±13.03
DBP (mmHg)	65.33±8.14	66.82±9.65	63.83±6.15	66.70±9.53	66.67±9.51
Hb (g/l)	135.65±17.97	137.86±16.04	148.25±23.03	137.53±16.14	137.64±16.24
UA (μmol/l)	331.89±97.72 [*]	307.61±83.36	388±125.73 [†]	309.26±84.40	310.06±85.16
TC (mmol/l)	4.22±0.87 [*]	3.84±0.67	5.67±0.98 [†]	3.86±0.68	3.88±0.70
HDL (mmol/l)	1.58±0.80	1.42±0.50	1.39±0.17	1.44±0.54	1.44±0.54
LDL (mmol/l)	2.35±0.73	2.19±0.91	3.38±0.66 [†]	2.19±0.89	2.20±0.89
TG (mmol/l)	1.28±1.26 [*]	0.97±0.59	2.11±1.98	0.99±0.67	1.00±0.70
Scr (mg/dl)	0.92±0.15 [*]	0.80±0.14	1.14±0.13 [†]	0.81±0.14	0.81±0.15
eGFR (ml/min/1.73 m ²)	84.28±7.04 [*]	110.16±13.70	66.19±6.07 [†]	107.97±14.80	107.55±15.31

Data are means ± SD or n (%);

^{*} Significantly different from subjects with eGFR 90 ml/min/1.73 m² (P<0.05);[†] Significantly different from subjects with eGFR 75 ml/min/1.73 m² (P<0.05).

Table 3

Logistic regression analysis of the factors related to childhood decreased eGFR.

	eGFR < 90 ml/min/1.73 m ² (n=80)		eGFR < 75 ml/min/1.73 m ² (n=8)
	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)
Age, years	0.91(0.84-0.98)	0.89(0.82-0.97)	–
Hyperuricemia ^b			
No ^r	1.00	1.00	–
Yes	1.64 (1.01-2.66)	1.96 (1.17-3.27)	–
Elevated TC			
No ^r	1.00	1.00	1.00
Yes	5.29 (2.52-11.11)	4.96 (2.28-10.80)	78.21 (15.13-404.27)
Elevated LDL			
No ^r	1.00	–	1.00
Yes	3.64 (1.63-8.13)	–	26.07 (6.21-109.44)
Dyslipidemia			
No ^r	1.00	–	1.00
Yes	2.22 (1.30-3.79)	–	16.63 (3.32-83.34)

- Not significant;

^r reference category;

^bUA 357μmol/l; demographic variables (age, gender and residence), general obesity, abdominal obesity, anaemia, hypertension, hyperuricemia, low HDL, elevated LDL, elevated TC, elevated TG and dyslipidemia were included in the adjusted model.