BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-044905
Article Type:	Original research
Date Submitted by the Author:	17-Sep-2020
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Keywords:	PUBLIC HEALTH, EPIDEMIOLOGY, RHEUMATOLOGY

Association between urbanization and the risk of hyperuricemia among Chinese adults: Findings from the China Health and Nutrition Survey

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Key words: urbanization, hyperuricemia, the China Health and Nutrition Survey

Conflict of interest: The authors have declared that no competing interests exist.

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Running title: urbanization and hyperuricemia

Word counts:2607

Abstract:232

number of references:40

number of figures and tables:5

No additional data available.

Abstract

Background

Hyperuricemia (HUA) has attracted worldwide concerns with its increasing prevalence. Few studies have revealed the association between urbanicity and HUA. The objective of this study is to explore whether urbanicity is an independent risk factor of HUA in Chinese adults.

Methods

The data we analyzed was extracted from the 2009 wave of the China Health and Nutrition Survey. The population included 8579 participants aged 18 years or older. According to urbanization index, we divided them into three categories (low, medium and highly urbanized groups). HUA was defined as serum uric acid ≥7 mg/dL in men and ≥6 mg/dL in women.

Results

The prevalence of HUA in low, medium and highly urbanized groups were 12.2%, 14.6% and 19.8%, respectively. The independent factors influencing

serum uric acid included age, gender, hypertension, diabetes, chronic kidney disease, drinking, obesity and community-level urbanization index. The risk of HUA in highly urbanized group was significantly higher than that of the low urbanized group (OR 1.661, 95%CI 1.246-2.212, P=0.001). In subgroup analysis, we found that age, gender, comorbidity (such as hypertension, diabetes, obesity and chronic kidney disease) and physical activities could affect the association between urbanization and the risk of HUA.

Conclusions

Our findings suggest that living in highly urbanized area is linked with higher risk of hyperuricemia independently of cardiometabolic and health-related behavioral risk factors, which have been shown to increase along with urbanization.

Strengths and limitations of this study

- This study explored the associations between urbanization and the risk of hyperuricemia in adults that few studies had reported.
- The data was extracted from the 2009 wave of the China Health and Nutrition Survey including 8579 participants, represented 47% of China's population and we found living in highly urbanized area is linked with higher risk of hyperuricemia independently of other covariates, especially in males without traditional hyperuricemia risk factors.

- This association in female group could be unavoidably affected when controlling for potential confounders in the binary logistics regression model, because the data of smoking in females missed a lot.
- Self-reported prevalence based on doctor diagnosis could be lower than the real prevalence of hypertension, diabetes mellitus, etc. and could affect the effects of urbanization.

Introduction

In recent decades, with the changes in diet and lifestyle as the economy develops, the prevalence of hyperuricemia(HUA) increases rapidly[1], which was reported to be strongly associated with many diseases, such as cardiovascular disease[2], diabetes mellitus[3], hypertension[4], dyslipidemia[5], and chronic kidney disease[6]. According to a previous study, the prevalence of hyperuricemia in Chinese adults was 13.3% in 2014[7].

Urbanicity was confirmed to have an influence on health through nutrition and lifestyle choices, pollution, occupational and traffic hazards, sanitary condition such as health-care access and vaccination coverage[8, 9]. Several studies have found that pollution[10], drinking[11], smoking[12], reduced physical activity[13, 14], were all associated with HUA. Furthermore, some studies have found that urbanicity was related to renal function[15, 16].The cause of HUA includes increased urate generation, decreased urate excretion and both of the two. Two-thirds of the urate is excreted through the kidney into urine and the remaining one-third is excreted via the ‘extra renal excretion’ pathway[17]. Reduced renal function can significantly increase the risk of hyperuricemia[18]. Then, whether urbanicity is a risk factor of HUA or not? Few studies had reported the relationship between urbanicity and HUA.

To explore the association between urbanicity and hyperuricemia, we used data from the China Health and Nutrition Survey (CHNS) and designed a multilevel model to explore whether urbanicity is an independent risk factor of hyperuricemia.

Materials and Methods

Sampling and Participants

Sampling in the present study came from the survey of China Health and Nutrition Survey (CHNS) in 2009.The CHNS is a longitudinal study of nine Chinese provinces (Guizhou, Guangxi, Heilongjiang, Henan, Hubei, Hunan, Liaoning, Jiangsu and Shandong). Nine surveys have been conducted since 1989. By 2011, the provinces included in the CHNS sample represented 47% of China's population (according to the census of 2010). The CHNS was designed to provide representation of urban, suburban and rural areas, varying significantly in economic development, public resources, geography and health indicators, and to focus on health during urbanization and economic change[19]. We selected a stratified probability sample from the nine provinces using a multistage, random-cluster design. Using this sampling strategy, we selected two cities (one large city, usually the provincial capital, and one small city, usually a lower income city) and four counties (stratified by income: one high, one low, and two middle-income counties). Within cities, we randomly selected two urban and two suburban communities; within counties, we randomly selected one community in the capital city and three rural villages. In each community, we selected 20 households in random and all household members were interviewed. The 2009 wave consisted of 216 communities and included 36 urban neighborhoods, 36 suburban neighborhoods, 36 towns and 108 villages. Current study population included 8579 participants aged 18 years or older and the selection procedures are depicted in Figure 1.

Urbanicity scale

Urbanicity was defined using a 12-component index capturing community-level physical, social, cultural and economic environments designed and validated for the CHNS[20]. The following 12 components were included in the development of the urbanization index:1.population density; 2.types of economic activity; 3.traditional market; 4.modern markets; 5.transportation and infrastructure; 6.sanitation;7.communications (e.g., TV, mobile, post, and cinema); 8.housing (e.g., electricity, indoor tap water, and flush toilet); 9. education;10.diversity (i.e., variation in community education level and variation in community income level); 11.health infrastructure; and 12.social services. This scale represents abroad-based measure of the elements of modernization that have potential health effects. Heterogeneity was captured by components in the presence/absence or number of facilities within the community, access to media or infrastructure, facility characteristics and the average proportion of individuals and households having a specific education or income level. From the CHNS household responses, we obtained the variables measuring proportion of households. Furthermore, from the CHNS community-level survey offered to community officials, we derived the remaining variables As described by Jones-Smith and Popkin, scoring distributions were variable across components, so they set the median score in a middle year as half the total points and each of the components was scaled to 0–10. Each component was then weighted equally in the overall index and added together for an overall maximum possible score of 120. This scale has been validated for content validity, reliability (α=0.85~0.89 across all study years), and stability across study years(r=0.90~0.94).

Definition of hyperuricemia

After at least 12 hours of overnight fasting, blood sample was collected by venipuncture in the morning. 4 ml of the blood sample was collected into a tube with separating gel, and was centrifuged 30 min after blood collection, at 3000× g for 15 min; the serum sample obtained from the centrifugation was frozen and stored at -86°C for later laboratory analysis. Another blood sample (500μL) was collected into a tube with EDTA for routine blood examination. All samples were verified and analyzed in a national central lab in Beijing (medical laboratory accreditation certificate ISO 15189:2007) according to strict quality control standard[21-23]. Serum uric acid (SUA) concentrations were measured with the use of an enzymatic colorimetric method on a Hitachi 7600 automated analyzer (Hitachi Inc., Tokyo, Japan) by determiner regents (Randox Laboratories Ltd., Crumlin, UK). HUA was defined as SUA concentrations ≥7 mg/dL in men and ≥6 mg/dL in women[1, 24-26].

Assessment of covariates

Self-reported medical history including hypertension, diabetes mellitus or high blood sugar, and life style information such as smoking, drinking was collected by trained interviewers. Hypertension was defined as either systolic pressure ≥ 140 mmHg, diastolic pressure ≥ 90 mmHg or self-reported diagnosis of hypertension[27]. Diabetes mellitus (DM) was defined as either fasting blood glucose ≥126 mg/dL (7.0 mmol/L) or glycosylated hemoglobin ≥ 6.5% or self-reported diagnosis of DM[28]. High level of low-density lipoprotein cholesterol (LDL-c) was defined as ≥3.12 mmol/L[29]. To accurately estimate the kidney function, we referred to CKD-EPI equation to calculate the estimated glomerular filtration rate (eGFR): $eGFR = 141 \times \min(SCr/\kappa, 1)^{\alpha} \times \max(SCr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.021$ [if female] $\times 1.159$ [if black], where SCr is serum creatinine, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of SCr/κ or 1, and max indicates the maximum of SCr/κ or 1[30]. Chronic kidney disease(CKD) was defined as eGFR < 60 ml/min/1.73 m^2 according to Kidney Disease: Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease[30]. From physical examination, we obtained the participants' body weight and height. Body mass index (BMI) was calculated as weight(kg) divided by height squared, and was classified into normal (BMI< 28.0), and obese (BMI ≥ 28.0)[31].

Physical activity included domestic activity(such as washing clothes, buying food for the family), occupation activity, transportation activity (such as walking to work or going to work by car), leisure activity (such as Kung fu, swimming, playing football)[32, 33], which was estimated by metabolic equivalent for task (MET). MET is a unit that estimates the amount of energy used by the body during physical activity, as compared to resting metabolism. The unit is standardized so it can apply to people of varying body weight and compare different activities[34]. The data of alcohol consumption and smoking situation of the participants also could be attained from CHNS and was classified into "yes" (≥ once per week) and "no" (<once per week) in our analysis.

Statistical analysis

Continuous variables were presented as means ± standard deviation (SD), while frequencies and percentages were used as categorical variables. The one-way ANOVA test (for continuous variables) and χ2 tests (for categorical variables) were used to compare the difference of HUA, age, gender, cardiometabolic risk factors (hypertension, diabetes mellitus, high level of LDL-c, obesity, CKD) and health-related behaviors (drinking, smoking, physical activity) among groups, respectively. And then the associations of uric acid with variables were tested using Spearman correlation coefficients in unadjusted and multivariable-adjusted linear regression models.

The method of maximum likelihood by the binary logistics regression model, was used to analyze the relationship between the risk of HUA in adulthood and community-level urbanization exposure. In the multivariable logistic regression model, we adjusted for age, gender, CKD, health-related behaviors and cardiometabolic risk factors. Model 1 was only controlled by age and gender, Model 2 was controlled for factors from model 1 plus cardiometabolic risk factors (obesity, hypertension, DM, high LDL, obesity and CKD). For Model 3, health-related behaviors (smoking, drinking, physical activity) were added for adjustment. All statistical analysis was conducted using the Statistical Package for the Social Sciences 13.0(SPSS Inc., Chicago, IL, USA). The data was demonstrated as odds ratio (OR) and 95% confidence interval (CI). A two-side p value <0.05 was considered significant.

Results

Characteristics of participants by tertiles of community-level urbanization index

A total of 8579 participants were enrolled into the current study. Basic characteristics of the participants are presented in Table 1. Since the community-level urbanization indexes ranged from 30.4 to 106.6, all participants were divided into low (<55.01), medium (>=55.01 and <82.33) and highly (>=82.33) urbanized groups by their community-level urbanization index tertiles accordingly. The prevalence of HUA rose with the urbanization scale (from 12.2% to 14.6% to 19.8%, $p<0.001$), the same as the trend of mean SUA levels (from 5.02 to 5.16 to 5.42, $p<0.001$).

With the increasing of the urbanization index, renal function declined dramatically (eGFR reduced from 81.98 to 78.71 to 76.57, $p<0.001$). In terms of cardiometabolic risk factors, subjects who lived in more urbanized communities were prone to hypertension, diabetes mellitus, high LDL-c and obesity. For the perspective of health-related behaviors, those subjects from higher urbanized areas tended to smoke less, drink less and be less physically active compared with lower urbanized areas.

Risk factors associated with serum uric acid among Chinese adults

Table2 shows the results of the univariable and multivariable linear regression analyses between serum uric acid and age, gender, cardiometabolic risk factors and health-related behaviors. The independent factors influencing serum uric acid included age, gender, hypertension, DM, obesity, CKD, drinking, and community-level urbanization index. Males, drinking individuals, individuals with cardiometabolic risk factors (such as hypertension, diabetes, obesity and CKD), and individuals who lived in a community with higher urbanization index tended to have higher serum uric acid.

Association of urbanization and the risk of hyperuricemia among Chinese adults

The association of urbanization with HUA in Chinese adults is demonstrated in Table 3. Compared with low urbanized group, the prevalence of HUA in medium and highly urbanized groups showed significant difference in univariate analysis, as shown in Table 1. We found even after adjusted by age, gender, cardiometabolic risk factors and health-related behaviors, the highly urbanized group still had higher risk of HUA compared with low urbanized group (OR 1.661, 95%CI 1.246-2.212, P=0.001). Furthermore, by subgroup analysis of the low and highly urbanized, age, gender, comorbidities (such as hypertension, diabetes, obesity and CKD) and physical activity were suggested to affect the association between urbanization and the risk of HUA (Figure 2). Young and middle-aged males living in the community with higher community-level urbanization index were prone to higher risk of HUA. Such association also existed in individuals without hypertension, diabetes, obesity or CKD and individuals with less physical activity.

Discussion

In the current study, we found that individuals living in higher urbanized areas were prone to higher risk of HUA. The association between urbanicity and HUA still remained after adjusted age, gender, cardiometabolic and health-related behavioral risk factors.

Several potential mechanisms could explain the associations between high urbanicity and HUA. High urbanicity means high pollution. There is larger amount of motor vehicles in highly urbanized areas, and the vehicle emissions including ozone and respirable particles contribute to air pollution. For example, in highly urbanized area like Beijing, motor vehicles grows by more than 1000 per day (mainly produced from coal) which would lead severe air pollution[35]. Previous studies have confirmed that the air pollution contained toxic organic agents including polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs), perfluorinated alkyl substances(PFASa), and dioxins, which could increase serum uric acid concentrations and the incidence of HUA[36]. Exposure to greater concentrations of long-term ambient air pollutants has been confirmed to be associated with a higher incidence of hyperuricemia[10].

High urbanicity is accompanied with less physical activity. As found in our study, the physical activity declined with the increase of urbanicity. In high urbanized areas, occupational physical activity is less common, as well as the transportation and domestic activity, as the popularization of motorized transport and labor-saving household appliances[37]. Physical exercise is closely interacted with serum uric acid. It was reported that SUA of the professional endurance athletes were significantly lower than non-athletes[38]. After aerobic exercise, serum uric acid increased immediately and then decreased to a level even lower than pre-exercise level[39], because energy-rich purine phosphates are transiently accumulated and catabolized, following by the lasting-long depletion. In our study, we also confirmed that, with adequate physical activities, individuals living in lower and higher urbanized communities have comparative risk of HUA.

High urbanicity means worse kidney function. A study including a large amount of population revealed that the higher risk of CKD in the higher urbanicity community[40]. Kidney is the most important organ to excrete uric acid and kidney function is closely related to SUA.

Urbanization has close association with other non-communicable diseases, such as diabetes, hypertension, high LDL-c, cardiovascular disease, cancer, and neuropsychiatric disorders with the changes in patterns of human activity, diet, and social structures in China[9]. These diseases can also increase the risk of HUA in some specific ways[1-4].

In addition, we also found that age, gender, comorbidity (such as hypertension, diabetes, obesity and CKD) and physical activity could affect the association between urbanization and the risk of HUA. Young and middle-aged men living in the community with high community-level urbanization index are prone to higher risk of HUA. Such association also exists in individuals without hypertension, diabetes, obesity and CKD and in individuals with less physical activity, suggesting that in high urbanized area, individuals without traditional HUA risk factors still have higher risk of HUA. The interaction between urbanicity and hypertension, diabetes, obesity and CKD might conceal the relationship between urbanicity and HUA in these subgroups.

The strengths of our study are : first, the data we analyzed in our survey was extracted from the CHNS including nine provinces which are widely representative of the entire Chinese mainland. Second, the innovative grouping and stratifying methods make it clarified to distinguish the exact stage in which urbanicity exerts influences on HUA.

Our study also has some findings counter-intuitive. First, elderly individuals in our study tend to have lower serum uric acid. Reduced kidney function, hypertension and diabetes could increase the risk of HUA, and are common in elderly individuals. However, elderly individuals usually diet less purine-rich food, pay more attention to health-related diet and behaviors than young individuals. Effective diet control can reduce serum uric acid by 60~70μmol/L, which can partly explain the relationship between age and serum uric acid. Second, the association between urbanicity and HUA after adjusting cardiometabolic and health-related behavioral risk factors only exists in men. For the perspective of health-related behaviors, female individuals tend to smoke less, drink less and be more inactive compared with male individuals.

In conclusion, living in high urbanized area is linked with higher risk of hyperuricemia independently of health-related behavioral and cardiometabolic risk factors, especially in individuals without traditional HUA risk factors, such as hypertension, diabetes mellitus, obesity or CKD.

Acknowledgements

We would like to acknowledge the team of the National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention, the Carolina Population Center, University of North Carolina at Chapel Hill, and the China–Japan Friendship Hospital, Ministry of Health who conducted the China Health and Nutrition Survey 2009. And we also acknowledge all the participants included in this study.

Ethics

The research was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill, the China-Japan Friendship Hospital and the Chinese Center for Disease Control and Prevention's National Institute for Nutrition and Health. All subjects gave informed consent for participation. The work presented in this paper was approved by the ethics committee of Zhongshan Hospital and the approval number is B2018-166.

Patient and Public Involvement statement

Patients and public will not be involved in the development of the research question or in the design of the study. Patients will receive oral and written information about this research; however, they will not be involved in the recruitment and conduct of the study. After signing an informed consent by the participants, they will be assessed for eligibility and data collection will begin. Dissemination of the general results (no personal data) will be made on demand.

Contributors

ZXY and DXQ were co-investigators and designed the study, YXX, ZH and SZY carried out the initial analysis, and supervised data analysis. All authors were involved in writing the paper and had final approval of the submitted and published versions.

Data sharing statement

The datasets analyzed in the current study are available online (https://www.cpc.unc.edu/projects/china).

Competing Interests: None

Funding

This study was supported by research grants from the Ministry of Science and Technology of People's Republic of China (2016YFC1305500), Shanghai

Municipal Health Commission (2017ZZ01015), and the China National Natural Scientific Foundation (81700646 and 81970637). The funders had no roles in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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Table 1 Basic characteristics of participants according to community-level urbanization index

Variables	Low urbanized	Medium urbanized	Highly urbanized	*P* value
Number	3554	2162	2863	
SUA, mean (*SD*), μmol/L	5.02(1.69)	5.16(1.75)	5.42(1.87)	<0.001
HUA, *n (%)*	435(12.2)	316(14.6)	567(19.8)	<0.001
Age, mean (*SD*), year	50.29(14.76)	50.50(14.94)	52.15(15.37)	<0.001
Male, *n (%)*	1696(47.7)	1020(47.2)	1324(46.3)	0.549
Hypertension, *n (%)*	1169(32.9)	753(34.8)	1069(37.3)	0.001
DM, *n (%)*	296(8.3)	258(11.9)	374(13.1)	<0.001
High LDL-c, *n (%)*	1209(34.6)	1000(46.3)	1261(44.0)	<0.001
Obesity, *n (%)*	298(8.4)	212(9.8)	312(10.9)	<0.001
eGFR, mean (*SD*), mL/min per 1.73 m^2	81.98(16.46)	78.71(16.88)	76.57(16.94)	<0.001
CKD, *n (%)*	307(8.6)	255(11.8)	437(15.3)	<0.001
Smoking, *n (%)*	1108(31.2)	558(25.8)	708(24.7)	<0.001
Drinking, *n (%)*	791(22.3)	458(21.2)	536(18.7)	<0.001
Physical activity, mean (*SD*), METs	125.48(123.73)	81.53(101.49)	51.71(72.26)	<0.001

Continuous variables were expressed as the mean ± SD and categorical variables were described as frequencies and percentages. The one-way ANOVA test (for continuous variables) and χ2 tests (for categorical variables) were used to compare the difference between different group. SUA, serum uric acid; HUA: hyperuricemia; DM, Diabetes mellitus; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate; CKD chronic kidney disease; MET, metabolic equivalent for task.

Table 2 Factors associated with serum uric acid among Chinese adults

	Univariable		Multivariable	
	β coefficient	***P* value**	**β coefficient**	**Adjusted *P* value**
Age (every 10 years)	0.019	<0.001	-0.028	<0.001
Gender (male *vs.* female)	0.287	<0.001	0.290	<0.001
Hypertension (yes *vs.* no)	0.110	<0.001	0.047	<0.001
DM (yes *vs.* no)	0.124	<0.001	0.067	<0.001
High LDL-c (yes *vs.* no)	0.031	<0.001	0.004	0.743
Obesity (yes *vs.* no)	0.133	<0.001	0.089	<0.001
CKD (yes *vs.* no)	0.195	<0.001	0.198	<0.001
Smoking (yes *vs.* no)	-0.018	0.307	-	-
Drinking (yes *vs.* no)	0.063	<0.001	0.037	0.001
Physical activity (every 10 METs)	<0.001	0.700	-	-
Community-level urbanization index (every 10 points)	0.016	<0.001	0.016	<0.001

The β coefficients and P values are from univariable and multivariable linear regression models of natural log-transformed uric acid as the dependent variable. The multivariable model included all covariates.DM, diabetes mellitus; LDL-c, low-density lipoprotein cholesterol; CKD, chronic kidney disease; MET, metabolic equivalent for task; –, without significance.

Table 3 Association of urbanization and the risk of hyperuricemia among Chinese adults

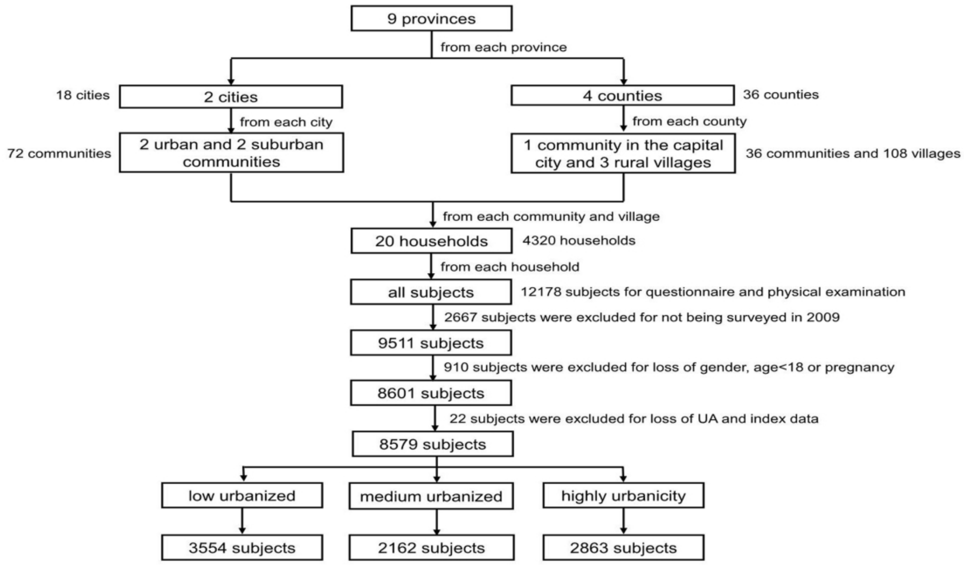
hyperuricemia (%)	12.2	14.6	19.8
P[1]		0.009	<0.001
Odds ratio (95% CI)[1]	Ref.	1.234(1.055-1.445)	1.767(1.539-2.028)
P[2]		0.218	<0.001
Odds ratio (95% CI)[2]	Ref.	1.109(0.941-1.308)	1.548(1.339-1.789)
P[3]		0.363	0.001
Odds ratio (95% CI)[3]	Ref.	1.160(0.842-1.599)	1.661(1.246-2.212)

[1]Model 1 was only controlled by age, gender.[2]Model 2 was controlled by hypertension, diabetes mellitus and high low-density lipoprotein, obesity and chronic kidney disease based on Model 1.[3]Model 3 was controlled by health-related behaviors (smoking, drinking, physical activity) based on Model 2.

Figure Legend

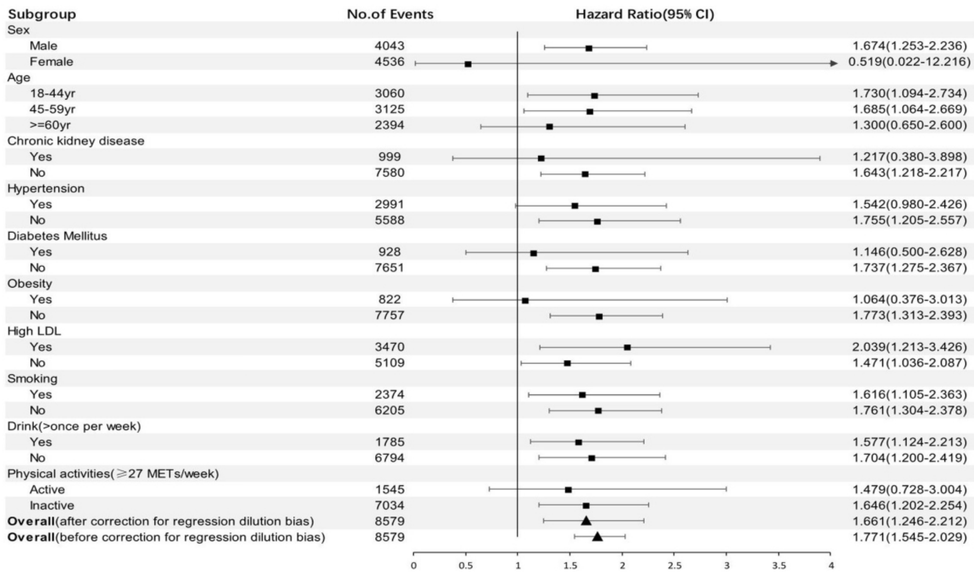
Figure1 Flowchart of the sample selecting methods at each step.

Figure2 Adjusted odds ratios for hyperuricemia with high urbanicity according to baseline characteristics. Analyses were adjusted for age, gender, hypertension, diabetes mellitus, high LDL (high low-density lipoprotein), obesity, chronic kidney disease, smoking, drinking and physical activity, as appropriate. The square black boxes represent odds ratios, and the horizontal lines represent 95% confidence intervals. The triangle black boxes represent the overall odds ratios and 95% confidence intervals.



Flowchart of the sample selecting methods at each step

169x99mm (600 x 600 DPI)



Adjusted odds ratios for hyperuricemia with high urbanicity according to baseline characteristics.

169x99mm (600 x 600 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6-8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	10
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	10
		(*e*) Describe any sensitivity analyses	10
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11
		(b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers of outcome events or summary measures	11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-12

		(*b*) Report category boundaries when continuous variables were categorized	11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	12
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17-18

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Association between urbanization and the risk of hyperuricemia among Chinese adults: a cross-sectional study from the China Health and Nutrition Survey (CHNS)

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-044905.R1
Article Type:	Original research
Date Submitted by the Author:	04-Dec-2020

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Primary Subject Heading:	Public health
Secondary Subject Heading:	Epidemiology
Keywords:	PUBLIC HEALTH, EPIDEMIOLOGY, RHEUMATOLOGY

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Association between urbanization and the risk of hyperuricemia among Chinese adults: a cross-sectional study from the China Health and Nutrition Survey (CHNS)

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Key words: urbanization, hyperuricemia, the China Health and Nutrition Survey

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Running title: urbanization and hyperuricemia

Word counts:2716

Abstract:240

number of references:52

number of figures and tables:5

No additional data available.

Abstract

Objectives To explore the association between urbanicity and hyperuricemia (HUA) and whether urbanicity is an independent risk factor of HUA in Chinese adults.

Design Data analysis from a cross-sectional survey.

Setting and participants 8579 subjects aged 18 years or older were enrolled in the study from the 2009 wave of the China Health and Nutrition Survey to analyze the association between urbanicity and hyperuricemia. According to urbanization index, we divided them into three categories (low, medium, and highly urbanized groups).

Main outcome measures HUA was defined as serum uric acid ≥7 mg/dL in men and ≥6 mg/dL in women.

Results The prevalence of HUA in low, medium, and highly urbanized groups were 12.2%, 14.6% and 19.8%, respectively. The independent factors influencing serum uric acid included age, gender, hypertension, diabetes, chronic kidney disease, drinking, obesity and community-level urbanization index(β =0.016, p<0.001).The risk of HUA in highly urbanized group was significantly higher than that of the low urbanized group (OR 1.771, 95%CI 1.545-2.029, P<0.001), even after adjusting for other covariates (OR 1.661, 95%CI 1.246-2.212, P=0.001). In subgroup analysis, we found that age, gender, comorbidity (such as hypertension, diabetes, obesity, and chronic kidney disease) and physical activities could affect the association between urbanization and the risk of HUA.

Conclusions Our findings suggest that living in highly urbanized area is linked with higher risk of hyperuricemia independently of cardiometabolic and health-related behavioral risk factors, which have been shown to increase along with urbanization.

Strengths and limitations of this study

- The present study used the 2009 wave of the China Health and Nutrition Survey represented 47% of China's population.
- Regression models were used to explore the associations between urbanization and the risk of hyperuricemia in Chinese adults.
- The association in female group could be unavoidably affected because a fair amount of smoking data was missing.
- Even with self-reported history, physical and laboratory examination, the real prevalence of hypertension, diabetes mellitus might be underestimated.

Introduction

In recent decades, with the changes in diet and lifestyle as the economy develops, the prevalence of hyperuricemia(HUA) increases rapidly[1]. In 2014, the prevalence of hyperuricemia in Chinese adults was 13.3% [2]. Hyperuricemia is not only an independent risk factor for new-onset chronic kidney disease (CKD)[3], but is also for CKD progression[4, 5]. Males and females with hyperuricemia have an increase in the risk of end-stage renal disease for 4 and 9 times, respectively[6]. Furthermore, hyperuricemia was reported to increase the risk of diabetes mellitus [7], hypertension[8], dyslipidemia[9], and cardiovascular events, especially sudden cardiac death[10, 11].

Urbanicity was confirmed to have an influence on health through nutrition and lifestyle choices, pollution, occupational and traffic hazards, sanitary condition such as health-care access and vaccination coverage[12, 13]. Several studies have found that pollution[14], drinking[15], smoking[16], reduced physical activity[17, 18], fructose intake[19], were all associated with HUA. Furthermore, some studies have found that renal function was related to urbanicity [20, 21].The cause of HUA includes increased urate generation, decreased urate excretion and both of the two. Two-thirds of the urate is excreted through the kidney into urine [22]. Reduced renal function can significantly increase the risk of hyperuricemia[23, 24]. Then, whether urbanicity is an independent risk factor of HUA or not? Few studies had investigated the relationship between urbanicity and HUA.

To explore the association between urbanicity and hyperuricemia, we used data from the China Health and Nutrition Survey (CHNS) and designed a multilevel model to explore whether urbanicity is an independent risk factor of hyperuricemia.

Materials and Methods

Sampling and Participants

Sampling in the present study came from the survey of China Health and Nutrition Survey (CHNS) in 2009.The CHNS is a longitudinal study of nine Chinese provinces (Guizhou, Guangxi, Heilongjiang, Henan, Hubei, Hunan, Liaoning, Jiangsu and Shandong). Nine surveys have been conducted since 1989[25]. By 2011, the provinces included in the CHNS sample represented 47% of China's population (according to the census of 2010). The CHNS was designed to provide representation of urban, suburban and rural areas, varying significantly in economic development, public resources, geography and health indicators, and to focus on health during urbanization and economic change[26]. We selected a stratified probability sample from the nine provinces using a multistage, random-cluster design. Using this sampling strategy, from each province we selected two cities (one large city, usually the provincial capital, and one small city, usually a lower income city) and four counties (stratified by income: one high, one low, and two middle-income counties). Within cities, we randomly selected two urban and two suburban communities; within counties, we randomly selected one community in the capital city and three rural villages. In each community, we selected 20 households in random and all household members were interviewed. The 2009 wave consisted of 216 communities and included 36 urban neighborhoods, 36 suburban neighborhoods, 36 towns and 108 villages. Current study population included 8579 participants aged 18 years or older and the selection procedures are depicted in Figure 1.

Urbanicity scale

Urbanicity was defined using a 12-component index capturing community-level physical, social, cultural and economic environments designed and validated for the CHNS[26]. The following 12 components were included in the development of the urbanization index:1.population density; 2.types of economic activity; 3.traditional market; 4.modern markets; 5.transportation and infrastructure; 6.sanitation;7.communications (e.g., TV, mobile, post, and cinema); 8.housing (e.g., electricity, indoor tap water, and flush toilet); 9. education;10.diversity (i.e., variation in community education level and variation in community income level); 11.health infrastructure; and 12.social services. This scale represents abroad-based measure of the elements of modernization that have potential health effects. Heterogeneity was captured by components in the presence/absence or number of facilities within the community, access to media or infrastructure, facility characteristics and the average proportion of individuals and households having a specific education or income level. From the CHNS household responses, we obtained the variables measuring proportion of households. Furthermore, from the CHNS community-level survey offered to community officials, we derived the remaining variables as described by Jones-Smith and Popkin, scoring distributions were variable across components, so they set the median score in a middle year as half the total points and each of the components was scaled to 0~10 [27, 28]. Each component was then weighted equally in the overall index and added together for an overall maximum possible score of 120. This scale has been validated for content validity, reliability (α=0.85~0.89 across all study years), and stability across study years(r=0.90~0.94). Since the community-level urbanization indexes in the population we studied ranged from 30.4 to 106.6, all participants were divided into low (<55.01), medium (>=55.01 and <82.33) and highly (>=82.33) urbanized groups by their community-level urbanization index tertiles accordingly.

Definition of hyperuricemia

After at least 12 hours of overnight fasting, blood sample was collected by venipuncture in the morning. 4 ml of the blood sample was collected into a tube with separating gel, and was centrifuged 30 min after blood collection, at 3000× g for 15 min; the serum sample obtained from the centrifugation was frozen and stored at -86°C for later laboratory analysis. Another blood sample (500μL) was collected into a tube with EDTA for routine blood examination. All samples were verified and analyzed in a national central lab in Beijing (medical laboratory accreditation certificate ISO 15189:2007) according to strict quality control standard[29]. Serum uric acid (SUA) concentrations were measured with the use of an enzymatic colorimetric method on a Hitachi 7600 automated analyzer (Hitachi Inc., Tokyo, Japan) by determiner regents (Randox Laboratories Ltd., Crumlin, UK). HUA was defined as SUA concentrations ≥7 mg/dL in men and ≥6 mg/dL in women[1, 29-32].

Assessment of covariates

Self-reported medical history including hypertension, diabetes mellitus or high blood sugar, and lifestyle information such as smoking, drinking was collected by trained interviewers. Hypertension was defined as either systolic pressure ≥ 140 mmHg, diastolic pressure ≥ 90 mmHg or self-reported diagnosis of hypertension[33]. Diabetes mellitus (DM) was defined as either fasting blood glucose ≥126 mg/dL (7.0 mmol/L) or glycosylated hemoglobin ≥ 6.5% or self-reported diagnosis of DM[34]. High level of low-density lipoprotein cholesterol (LDL-c) was defined as ≥3.12 mmol/L[35]. To accurately estimate the kidney function, we referred to CKD-EPI equation to calculate the estimated glomerular filtration rate (eGFR): $eGFR = 141 \times \min(SCr/\kappa, 1)^{\alpha} \times \max(SCr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.021$ [if female] $\times 1.159$ [if black], where SCr is serum creatinine, κ is 0.7

for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of SCr/κ or 1, and max indicates the maximum of SCr/κ or 1[36]. Chronic kidney disease(CKD) was defined as eGFR < 60 ml/min/1.73 m^2 according to Kidney Disease: Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease[36]. From physical examination, we obtained the participants' body weight and height. Body mass index (BMI) was calculated as weight(kg) divided by height squared, and was classified into normal or overweight (BMI< 28.0kg/m^2), and obese (BMI ≥ 28.0 kg/m^2)[37].

Physical activity included domestic activity(such as washing clothes, buying food for the family), occupation activity, transportation activity (such as walking to work or going to work by car), leisure activity (such as Kung fu, swimming, playing football)[38, 39], which was estimated by metabolic equivalent for task (MET). MET is a unit that estimates the amount of energy used by the body during physical activity, as compared to resting metabolism. The unit is standardized so it can apply to people of varying body weight and compare different activities[40]. Active or inactive group was defined as ≥/< 27 METs/week according to the physical activity level[29].The data of alcohol consumption and smoking situation of the participants also could be attained from CHNS and was classified into "yes" (≥ once per week) and "no" (<once per week) in our analysis.

Statistical analysis

Continuous variables were presented as means ± standard deviation (SD), while frequencies and percentages were used as categorical variables. The one-way ANOVA test (for continuous variables) and χ2 tests (for categorical variables) were used to compare the difference of HUA, age, gender, cardiometabolic risk factors (hypertension, diabetes mellitus, high level of LDL-c, obesity, CKD) and health-related behaviors (drinking, smoking, physical activity) among groups, respectively. And then the associations of uric acid with variables were tested using Spearman correlation coefficients in unadjusted and multivariable-adjusted linear regression models.

The method of maximum likelihood by the binary logistics regression model, was used to analyze the relationship between the risk of HUA in adulthood and community-level urbanization exposure. In the multivariable logistic regression model, we adjusted for age, gender, CKD, health-related behaviors and cardiometabolic risk factors. Model 1 was only controlled by age and gender, Model 2 was controlled for factors from model 1 plus cardiometabolic risk factors (obesity, hypertension, DM, high LDL, obesity and CKD). For Model 3, health-related behaviors (smoking, drinking, physical activity) were added for adjustment. All statistical analysis was conducted using the Statistical Package for the Social Sciences 13.0(SPSS Inc., Chicago, IL, USA). The data was demonstrated as odds ratio (OR) and 95% confidence interval (CI). A two-side p value <0.05 was considered significant.

Results

Characteristics of participants by tertiles of community-level urbanization index

A total of 8579 participants were enrolled into the current study. Basic characteristics of the participants are presented in Table 1. The prevalence of HUA rose with the urbanization scale (from 12.2% to 14.6% to 19.8%, p<0.001), the same as the trend of mean SUA levels (from 5.02 to 5.16 to 5.42, p<0.001). With the increasing of the urbanization index, renal function declined dramatically (eGFR reduced from 81.98 to 78.71 to 76.57, p<0.001). In terms of cardiometabolic risk factors, subjects who lived in more urbanized communities were prone to hypertension, diabetes mellitus, high LDL-c and obesity. For the perspective of health-related behaviors, those subjects from higher urbanized areas tended to smoke less, drink less and be less physically active compared with lower urbanized areas.

Risk factors associated with serum uric acid among Chinese adults

Table2 shows the results of the univariable and multivariable linear regression analyses between serum uric acid and age, gender, cardiometabolic risk factors and health-related behaviors. The independent factors influencing serum uric acid included age, gender, hypertension, DM, obesity, CKD, drinking, and community-level urbanization index. Males, drinking individuals, individuals with cardiometabolic risk factors (such as hypertension, diabetes, obesity and CKD), and individuals who lived in a community with higher urbanization index tended to have higher serum uric acid.

Association of urbanization and the risk of hyperuricemia among Chinese adults

The association of urbanization with HUA in Chinese adults is demonstrated in Table 3. Compared with low urbanized group, the prevalence of HUA in medium and highly urbanized groups showed significant difference in univariate analysis, as shown in Table 1. We found even after adjusted by age, gender, cardiometabolic risk factors and health-related behaviors, the highly urbanized group still had higher risk of HUA compared with low urbanized group (OR 1.661, 95%CI 1.246-2.212, P=0.001). Furthermore, by subgroup analysis of the low and highly urbanized, age, gender, comorbidities (such as hypertension, diabetes, obesity and CKD) and physical activity were suggested to affect the association between urbanization and the risk of HUA (Figure 2). Young and middle-aged males living in the community with higher community-level urbanization index were prone to higher risk of HUA. Such association also existed in individuals without hypertension, diabetes, obesity or CKD and individuals with less physical activity.

Discussion

In the current study, we found that individuals living in higher urbanized areas were prone to higher risk of HUA. The association between urbanicity and HUA still remained after adjusted age, gender, cardiometabolic and health-related behavioral risk factors.

What cause large regional differences in PM2.5 pollutions in China? Several potential mechanisms could explain the associations between high urbanicity and HUA. There is high pollution in highly urbanized area[41-43]. Previous studies had revealed that air pollution in China is mainly caused by population aggregation, urbanization, industrial discharges, outside investment, vehicle exhausts, coal consumption, technological development and straw burning[44, 45].And air pollution was reported to associate with lower eGFR and increased prevalence of CKD, thus increasing the risk of hyperuricemia[46]. Furthermore, previous studies have confirmed that the air pollution contained toxic organic agents including polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs), perfluorinated alkyl substances (PFASa), and dioxins, which could increase serum uric acid concentrations and the incidence of HUA[47]. Exposure to greater concentrations of long-term ambient air pollutants has been confirmed to be associated with a higher incidence of hyperuricemia[14].

High urbanicity is accompanied with less physical activity. As found in our study, the physical activity declined with the increase of urbanicity. In high urbanized areas, occupational physical activity is less common, as well as the transportation and domestic activity, as the popularization of motorized transport and labor-saving household appliances[48]. Physical exercise is closely interacted with serum uric acid. It was reported that SUA of the professional endurance athletes were significantly lower than non-athletes[49]. After aerobic exercise, serum uric acid increased immediately and then decreased to a level even lower than pre-exercise level[50], because energy-rich purine phosphates are transiently accumulated and catabolized, following by the lasting-long depletion. In our study, we also confirmed that, with inadequate physical activities, individuals living in high urbanized communities have higher risk of HUA.

High urbanicity means worse kidney function. A previous study including a large amount of population revealed that the higher risk of CKD in the higher urbanicity community[51]. And as we found in Table 1, the highly urbanized group had the highest prevalence of CKD. Kidney is the most important organ to excrete uric acid and kidney function is closely related to SUA, which was consistent with Table 2. The serum uric acid level of patients with CKD was higher than those without CKD.

Urbanization has close association with other non-communicable diseases, such as diabetes, hypertension, high LDL-c, cardiovascular disease, cancer, and neuropsychiatric disorders with the changes in patterns of human activity, diet, and social structures in China[13]. These diseases can also increase the risk of HUA in some specific ways[1, 7, 11, 52].

In addition, we also found that age, gender, comorbidity (such as hypertension, diabetes, obesity and CKD) and physical activity could affect the association between urbanization and the risk of HUA. Young and middle-aged men living in the community with high community-level urbanization index are prone to higher risk of HUA. Such association also exists in individuals without hypertension, diabetes, obesity and CKD and in individuals with less physical activity, suggesting that in high urbanized area, individuals without traditional HUA risk factors still have higher risk of HUA. The interaction between urbanicity and hypertension, diabetes, obesity and CKD might conceal the relationship between urbanicity and HUA in these subgroups.

The strengths of our study are: first, the data we analyzed in our survey was extracted from the CHNS including nine provinces which are widely representative of the entire Chinese mainland. Second, the innovative grouping and stratifying methods make it clarified to distinguish the exact stage in which urbanicity exerts influences on HUA.

Our study also has some limitations. First, elderly individuals in our study tend to have lower serum uric acid. Reduced kidney function, hypertension and diabetes could increase the risk of HUA, and are common in elderly individuals. However, elderly individuals usually diet less purine-rich food, pay more attention to health-related diets and behaviors than young individuals. Effective diet control can reduce serum uric acid by 60~70μmol/L, which can partly explain the relationship between age and serum uric acid. Second, the association between urbanicity and HUA only exists in men after adjusting cardiometabolic and health-related behavioral risk factors. This may be explained by that females tend to smoke less, drink less and be more inactive compared with males, thus their uric acid level is less influenced by urbanicity. Third, the association in female group could be unavoidably affected because a fair amount of smoking data was missing. Fourth, even with self-reported history, physical and laboratory examination, the real prevalence of hypertension, diabetes mellitus might be underestimated. Finally, the population we analyzed was derived from China, and global data is needed to generalize the result.

In conclusion, living in high urbanized area is linked with higher risk of hyperuricemia independently of health-related behavioral and cardiometabolic risk factors, especially in individuals without traditional HUA risk factors, such as hypertension, diabetes mellitus, obesity or CKD.

Acknowledgements

We would like to acknowledge the team of the National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention, the Carolina Population Center, University of North Carolina at Chapel Hill, and the China–Japan Friendship Hospital, Ministry of Health who conducted the China Health and Nutrition Survey 2009. And we also acknowledge all the participants included in this study.

Ethics

The CHNS was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill, the China-Japan Friendship Hospital and the Chinese Center for Disease Control and Prevention's National Institute for Nutrition and Health. All subjects gave informed consent for participation. The access to the data with approved by the above Institutional Review Board. The analysis of the data presented in this paper was approved by the Ethics Committee of Zhongshan Hospital, Fudan University (B2018-166).

Patient and Public Involvement statement

Patients and public had not been involved in the development of the research question or in the design of the study. Patients had received oral and written information about this research; however, they were not involved in the recruitment and conduct of the study. After signing informed consent, they were assessed for eligibility, and data collection began. Dissemination of the general results (no personal data) were approved only after the CHNS Review Board qualified the application.

Contributors

Zhang Xiaoyan and Ding Xiaoqiang were co-investigators and supervisors of the study. Yu Xixi carried out the study design, the data analysis and paper writing. Zhu Cheng provided the original idea of the paper, the original writing idea of the paper and played a vital role in revised submission. Zhang Han and Chen Jing served as scientific advisors and supervised data analysis. Shen Ziyan and Gu Yulu polished the article. Lv Shiqi, Zhang Di and Wang Yulin collected the data. All authors were involved in writing the paper and had final approval of the submitted and published versions.

Data sharing statement

The datasets analyzed in the current study are available online (https://www.cpc.unc.edu/projects/china).

Competing Interests: None declared.

Funding

This study was supported by research grants from the Ministry of Science and Technology of People's Republic of China (2016YFC1305500), Shanghai Municipal Health Commission (2017ZZ01015), and the China National Natural Scientific Foundation (81700646 and 81970637). The funders had no roles in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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Table 1 Basic characteristics of participants according to community-level urbanization index

Variables	Low urbanized	Medium urbanized	Highly urbanized	*P* value
Number	3554	2162	2863	
SUA, mean (*SD*), μmol/L	5.02(1.69)	5.16(1.75)	5.42(1.87)	<0.001
HUA, *n (%)*	435(12.2)	316(14.6)	567(19.8)	<0.001
Age, mean (*SD*), year	50.29(14.76)	50.50(14.94)	52.15(15.37)	<0.001
Male, *n (%)*	1696(47.7)	1020(47.2)	1327(46.3)	0.549
Hypertension, *n (%)*	1169(32.9)	753(34.8)	1069(37.3)	0.001
DM, *n (%)*	296(8.3)	258(11.9)	374(13.1)	<0.001
High LDL-c, *n (%)*	1209(34.6)	1000(46.3)	1261(44.0)	<0.001
Obesity, *n (%)*	298(8.4)	212(9.8)	312(10.9)	<0.001
eGFR, mean (*SD*), mL/min per 1.73 m^2	81.98(16.46)	78.71(16.88)	76.57(16.94)	<0.001
CKD, *n (%)*	307(8.6)	255(11.8)	437(15.3)	<0.001
Smoking, *n (%)*	1108(31.2)	558(25.8)	708(24.7)	<0.001
Drinking, *n (%)*	791(22.3)	458(21.2)	536(18.7)	<0.001
Physical activity, mean (*SD*), METs	125.48(123.73)	81.53(101.49)	51.71(72.26)	<0.001

Continuous variables were expressed as the mean ± SD and categorical variables were described as frequencies and percentages. The one-way ANOVA test (for continuous variables) and χ2 tests (for categorical variables) were used to compare the difference between different group. SUA, serum uric acid; HUA: hyperuricemia; DM, Diabetes mellitus; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate; CKD chronic kidney disease; MET, metabolic equivalent for task.

Table 2 Factors associated with serum uric acid among Chinese adults

	Univariable		Multivariable	
	β coefficient	***P* value**	**β coefficient**	**Adjusted *P* value**
Age (every 10 years)	0.019	<0.001	-0.028	<0.001
Gender (male *vs.* female)	0.287	<0.001	0.290	<0.001
Hypertension (yes *vs.* no)	0.110	<0.001	0.047	<0.001
DM (yes *vs.* no)	0.124	<0.001	0.067	<0.001
High LDL-c (yes *vs.* no)	0.031	<0.001	0.004	0.743
Obesity (yes *vs.* no)	0.133	<0.001	0.089	<0.001
CKD (yes *vs.* no)	0.195	<0.001	0.198	<0.001
Smoking (yes *vs.* no)	-0.018	0.307	-	-
Drinking (yes *vs.* no)	0.063	<0.001	0.037	0.001
Physical activity (every 10 METs)	<0.001	0.700	-	-
Community-level urbanization index (every 10 points)	0.016	<0.001	0.016	<0.001

The β coefficients and P values are from univariable and multivariable linear regression models of natural log-transformed uric acid as the dependent variable. The multivariable model included all covariates.DM, diabetes mellitus; LDL-c, low-density lipoprotein cholesterol; CKD, chronic kidney disease; MET, metabolic equivalent for task; –, without significance.

Table 3 Association of urbanization and the risk of hyperuricemia among Chinese adults

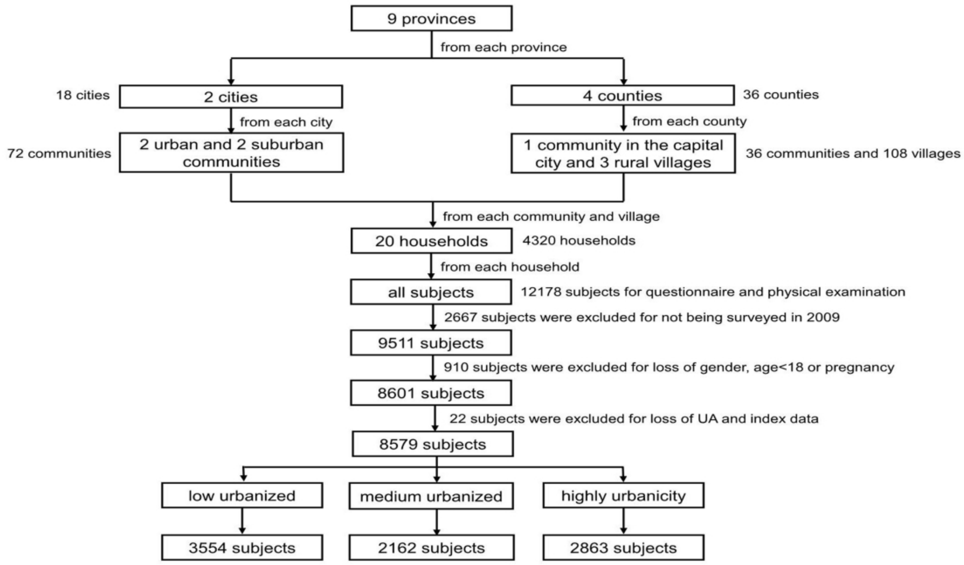
Variables	Low urbanized	Medium urbanized	Highly urbanized
hyperuricemia (%)	12.2	14.6	19.8
P[1]		0.009	<0.001
Odds ratio (95% CI)[1]	Ref.	1.234(1.055-1.445)	1.767(1.539-2.028)
P[2]		0.218	<0.001
Odds ratio (95% CI)[2]	Ref.	1.109(0.941-1.308)	1.548(1.339-1.789)
P[3]		0.363	0.001
Odds ratio (95% CI)[3]	Ref.	1.160(0.842-1.599)	1.661(1.246-2.212)

[1]Model 1 was only controlled by age, gender.[2]Model 2 was controlled by hypertension, diabetes mellitus and high low-density lipoprotein, obesity and chronic kidney disease based on Model 1.[3]Model 3 was controlled by health-related behaviors (smoking, drinking, physical activity) based on Model 2.

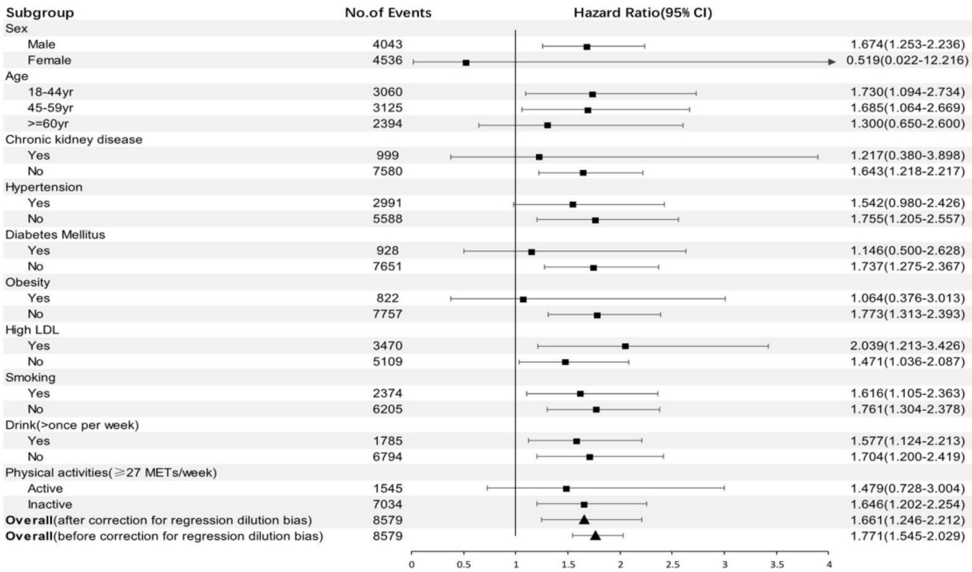
Figure Legend

Figure1 Flowchart of the sample selecting methods at each step.

Figure2 Adjusted odds ratios for hyperuricemia with high urbanicity according to baseline characteristics. Analyses were adjusted for age, gender, hypertension, diabetes mellitus, high LDL (high low-density lipoprotein), obesity, chronic kidney disease, smoking, drinking and physical activity, as appropriate. The square black boxes represent odds ratios, and the horizontal lines represent 95% confidence intervals. The triangle black boxes represent the overall odds ratios and 95% confidence intervals.



Flowchart of the sample selecting methods at each step



Adjusted odds ratios for hyperuricemia with high urbanicity according to baseline characteristics.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5-6
Methods			
Study design	4	Present key elements of study design early in the paper	6-11
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6-7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9-11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-11
Bias	9	Describe any efforts to address potential sources of bias	11
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-11
		(*b*) Describe any methods used to examine subgroups and interactions	11
		(*c*) Explain how missing data were addressed	11
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	11
		(*e*) Describe any sensitivity analyses	11
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6-7
		(b) Give reasons for non-participation at each stage	6-7
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12
		(b) Indicate number of participants with missing data for each variable of interest	7
Outcome data	15*	Report numbers of outcome events or summary measures	12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-13

		(*b*) Report category boundaries when continuous variables were categorized	12
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	13
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	16-17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Association between urbanization and the risk of hyperuricemia among Chinese adults: a cross-sectional study from the China Health and Nutrition Survey (CHNS)

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-044905.R2
Article Type:	Original research
Date Submitted by the Author:	04-Feb-2021
Complete List of Authors:	Yu, Xixi; Zhongshan Hospital Fudan University, Zhu, Cheng; Zhongshan Hospital Fudan University Zhang, Han; Zhongshan Hospital Fudan University, Nephrology Shen, Ziyan; Zhongshan Hospital Fudan University, Nephrology Chen, Jing; Zhongshan Hospital Fudan University, Nephrology Gu, Yulu; Zhongshan Hospital Fudan University, Nephrology Lv, Shiqi; Zhongshan Hospital Fudan University, Nephrology Zhang, Di; Zhongshan Hospital Fudan University, Nephrology Wang, Yulin; Zhongshan Hospital Fudan University, Nephrology Ding, Xiaoqiang; Zhongshan Hospital Fudan University, Nephrology Zhang, Xiaoyan; Zhongshan Hospital Fudan University, Nephrology
Primary Subject Heading:	Public health
Secondary Subject Heading:	Epidemiology
Keywords:	PUBLIC HEALTH, EPIDEMIOLOGY, RHEUMATOLOGY

Association between urbanization and the risk of hyperuricemia among Chinese adults: a cross-sectional study from the China Health and Nutrition Survey (CHNS)

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Key words: urbanization, hyperuricemia, the China Health and Nutrition Survey

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Running title: urbanization and hyperuricemia

Word count:2649

Abstract:240

Number of references:52

Number of figures and tables:5

No additional data available.

Abstract

Objectives To explore the association between urbanicity and hyperuricemia (HUA) and whether urbanicity is an independent risk factor of HUA in Chinese adults.

Design Data analysis from a cross-sectional survey.

Setting and participants 8579 subjects ages 18 years or older were enrolled in the study from the 2009 wave of the China Health and Nutrition Survey to analyze the association between urbanicity and hyperuricemia. We divided them into three categories according to urbanization index (low, medium, and highly urbanized groups).

Main outcome measures HUA was defined as serum uric acid ≥7 mg/dL in men and ≥6 mg/dL in women.

Results The prevalence of HUA in low, medium, and highly urbanized groups was 12.2%, 14.6%, and 19.8% respectively. The independent factors influencing serum uric acid included age, gender, hypertension, diabetes, chronic kidney disease, drinking, obesity, and community-level urbanization index(β =0.016, p<0.001).The risk of HUA in the highly urbanized group was significantly higher than that of the low urbanized group (OR 1.771, 95%CI 1.545-2.029, P<0.001), even after adjusting for other covariates (OR 1.661, 95%CI 1.246-2.212, P=0.001). In subgroup analysis, we found that age, gender, comorbidity (such as hypertension, diabetes, obesity, and chronic kidney disease), and physical activity affected the association between urbanization and the risk of HUA.

Conclusions Our findings suggest that living in highly urbanized areas is linked with higher risk of hyperuricemia independent of cardiometabolic and health-related behavioral risk factors, which have been shown to increase along with urbanization.

Strengths and limitations of this study

- The present study used the 2009 wave of the China Health and Nutrition Survey which represented 47% of China's population.
- Regression models were used to explore the associations between urbanization and the risk of hyperuricemia in Chinese adults.
- The association in the female group could be impacted due to a significant amount of missing smoking data.

- Even with self-reported history, physicals, and laboratory examinations, the real prevalence of hypertension and diabetes mellitus might be under-reported.

Introduction

In recent decades, with the changes in diet and lifestyle as the economy develops, the prevalence of hyperuricemia(HUA) has increased rapidly[1]. In 2014, the prevalence of hyperuricemia in Chinese adults was 13.3% [2]. Hyperuricemia is both an independent risk factor for new-onset chronic kidney disease (CKD)[3], as well as CKD progression[4, 5]. Males and females with hyperuricemia have four and nine times increase in the risk of end-stage renal disease, respectively[6]. Furthermore, hyperuricemia was reported to increase the risk of diabetes mellitus [7], hypertension[8], dyslipidemia[9], and cardiovascular events, especially sudden cardiac death[10, 11].

Urbanicity was confirmed to have an influence on health through nutrition and lifestyle choices, pollution, occupational and traffic hazards, and sanitary conditions such as health-care access and vaccination coverage[12, 13]. Several studies have found that pollution[14], drinking[15], smoking[16], reduced physical activity[17, 18],and fructose intake[19], were all associated with HUA. Furthermore, some studies have found that renal function was related to urbanicity [20, 21].The causes of HUA include increased urate generation, decreased urate excretion or a combination of both factors. Two-thirds of urate is excreted through the kidney into urine [22]. Reduced renal function can significantly increase the risk of hyperuricemia[23, 24].

Few studies had investigated the relationship between urbanicity and HUA. To explore this association, we used data from the China Health and Nutrition Survey (CHNS) and designed a multilevel model to explore whether urbanicity is an independent risk factor of hyperuricemia.

Materials and Methods

Sampling and Participants

Sampling in the present study came from the survey of China Health and Nutrition Survey (CHNS) in 2009. The CHNS is a longitudinal study of nine Chinese provinces (Guizhou, Guangxi, Heilongjiang, Henan, Hubei, Hunan, Liaoning, Jiangsu, and Shandong). Nine surveys have been conducted since 1989[25]. By 2011, the provinces included in the CHNS represented 47% of China's population according to the 2010 census. The CHNS was designed to provide representation of urban, suburban, and rural areas varying significantly in economic development, public resources, geography, and health indicators, and to focus on health during urbanization and economic change[26]. We selected a stratified probability sample from the nine provinces using a multistage, random-cluster design. Using this sampling strategy, we selected two cities from each province (one large city, usually the provincial capital, and one small city, usually a lower income city) and four counties (stratified by income: one high, one low, and two middle-income counties). Within cities, we randomly selected two urban and two suburban communities; within counties, we randomly selected one community in the capital city and three rural villages. In each community, we selected 20 households at random and all household members were interviewed. The 2009 wave consisted of 216 communities and included 36 urban neighborhoods, 36 suburban neighborhoods, 36 towns, and 108 villages. Current study population included 8579 participants ages 18 years and older and the selection procedures are depicted in Figure 1.

Urbanicity scale

Urbanicity was defined using a 12-component index capturing community-level physical, social, cultural, and economic environments designed and validated for the CHNS[26]. The following 12 components were included in the development of the urbanization index: 1. population density; 2. types of economic activity; 3. traditional market; 4. modern markets; 5. transportation and infrastructure; 6. sanitation; 7. communication and media (e.g., TV, mobile, post, and cinema); 8. housing (e.g., electricity, indoor tap water, and flushing toilets); 9. education; 10. diversity (i.e., variation in community education level and variation in community income level); 11. health infrastructure; 12. social services. This scale represents abroad-based factors of modernization that have potential health effects. Heterogeneity was captured by components in the presence/absence or number of facilities within the community, access to media or infrastructure, facility characteristics, and the average proportion of individuals and households having a specific education or income level. We obtained the variables measuring proportion of households from the CHNS responses. Using the CHNS community-level survey offered to community officials, we derived the remaining variables as described by Jones-Smith and Popkin. Scoring distributions were variable across components, so the median score in a middle year was designated as half the total points and each of the components was scaled from 0 to 10 [27, 28]. Each component was then weighted equally in the overall index and added together for an overall maximum possible score of 120. This scale has been validated for content validity, reliability (α=0.85~0.89 across all study years), and stability across study years(r=0.90~0.94). Since the community-level urbanization indexes in the population we studied ranged from 30.4 to 106.6, all participants were divided into low (<55.01), medium (>=55.01 and <82.33), and highly (>=82.33) urbanized groups by their community-level urbanization index tertiles accordingly.

Definition of hyperuricemia

After at least 12 hours of overnight fasting, a blood sample was collected by venipuncture in the morning. Four mL of the blood sample was collected into a tube with separating gel and was centrifuged 30 min after collection at 3000× g for 15 min; the serum sample obtained from the centrifugation was frozen and stored at -86°C for laboratory analysis. Another blood sample (500μL) was collected into a tube with EDTA for routine blood examination. All samples were verified and analyzed in a national central lab in Beijing (medical laboratory accreditation certificate ISO 15189:2007) according to strict quality control standard[29]. Serum uric acid (SUA) concentrations were measured with the use of an enzymatic colorimetric method on a Hitachi 7600 automated analyzer (Hitachi Inc., Tokyo, Japan) by determiner regents (Randox Laboratories Ltd., Crumlin, UK). HUA was defined as SUA concentrations ≥7 mg/dL in men and ≥6 mg/dL in women[1, 29-32].

Assessment of covariates

Self-reported medical history including hypertension, diabetes mellitus or high blood sugar, and lifestyle information such as smoking, and drinking was collected by trained interviewers. Hypertension was defined as either systolic pressure ≥ 140 mmHg, diastolic pressure ≥ 90 mmHg, or self-reported diagnosis of hypertension[33]. Diabetes mellitus (DM) was defined as either fasting blood glucose ≥126 mg/dL (7.0 mmol/L) or glycosylated hemoglobin ≥ 6.5%, or self-reported diagnosis of DM[34]. High level of low-density lipoprotein cholesterol (LDL-c) was defined as ≥3.12 mmol/L[35]. To accurately estimate kidney function, we referred to CKD-EPI equation to calculate the estimated glomerular filtration rate (eGFR): $eGFR = 141 \times \min(SCr/\kappa, 1)^{\alpha} \times \max(SCr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.021$ [if female] × 1.159 [if black], where SCr is serum creatinine, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of SCr/κ or 1, and max indicates the maximum of SCr/κ or 1[36]. Chronic kidney disease(CKD) was defined as eGFR < 60 mL/min/1.73 m^2 according to Kidney Disease: Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease[36]. From physical examination, we obtained the participants' body weight and height. Body mass index (BMI) was calculated as weight(kg) divided by height squared, and was classified into normal or overweight (BMI< 28.0kg/m^2), and obese (BMI ≥ 28.0 kg/m^2)[37]. Physical activity included domestic activity (such as washing clothes, grocery shopping), occupation activity, transportation activity (such as walking or driving to work), leisure activity (such as kung fu, swimming, playing football)[38, 39], which was estimated by metabolic equivalent for task (MET). MET is a unit that estimates the amount of energy used by the body during physical activity, relative to resting metabolism. The unit is standardized so it can apply to people of varying body weight participating indifferent activities[40]. Active or inactive group was defined as ≥/< 27 METs/week according to the physical activity level[29].The data of alcohol consumption and smoking status of the participants also could be attained from the CHNS and was classified as "yes" (≥ once per week) or "no" (<once per week) in our analysis.

Statistical analysis

Continuous variables were presented as means ± standard deviation (SD), while frequencies and percentages were used as categorical variables. The one-way ANOVA test (for continuous variables) and χ2 tests (for categorical variables) were used to compare the difference of HUA, age, gender, cardiometabolic risk factors (hypertension, diabetes mellitus, high level of LDL-c, obesity, CKD), and health-related behaviors (drinking, smoking, physical activity) among groups, respectively. Additionally, the associations of uric acid with variables were tested using Spearman correlation coefficients in unadjusted and multivariable-adjusted linear regression models.

The method of maximum likelihood by the binary logistics regression model was used to analyze the relationship between the risk of HUA in adulthood and community-level urbanization exposure. In the multivariable logistic regression model, we adjusted for age, gender, CKD, health-related behaviors, and cardiometabolic risk factors. Model 1 was only controlled by age and gender, Model 2 was controlled for factors from model 1 plus cardiometabolic risk factors (obesity, hypertension, DM, high LDL, obesity, and CKD). For Model 3, health-related behaviors (smoking, drinking, and physical activity) were added for adjustment. All statistical analysis was conducted using the Statistical Package for the Social Sciences 13.0(SPSS Inc., Chicago, IL, USA). The data was demonstrated as odds ratio (OR) and 95% confidence interval (CI). A two-side p value <0.05 was considered significant.

Results

Characteristics of participants by tertiles of community-level urbanization index

A total of 8579 participants were enrolled into the current study. Basic characteristics of the participants are presented in Table 1. The prevalence of HUA rose with the urbanization scale (from 12.2% to 14.6% to 19.8%, p<0.001), as did the trend of mean SUA levels (from 5.02 to 5.16 to 5.42, p<0.001).

As urbanization increased, renal function declined dramatically (eGFR reduced from 81.98 to 78.71 to 76.57, p<0.001). In terms of cardiometabolic risk factors, subjects who lived in more urbanized communities were prone to hypertension, diabetes mellitus, high LDL-c, and obesity. For the perspective of health-related behaviors, those subjects from highly urbanized areas tended to smoke less, drink less, and be less physically active compared with low urbanized areas.

Risk factors associated with serum uric acid among Chinese adults.

Table 2 shows the results of the univariable and multivariable linear regression analyses between serum uric acid and age, gender, cardiometabolic risk factors, and health-related behaviors. The independent factors influencing serum uric acid included age, gender, hypertension, DM, obesity, CKD, drinking, and community-level urbanization index. Males, drinking individuals, individuals with cardiometabolic risk factors (such as hypertension, diabetes, obesity, and

CKD), and individuals who lived in a community with higher urbanization index tended to have higher serum uric acid.

Association of urbanization and the risk of hyperuricemia among Chinese adults

The association of urbanization with HUA in Chinese adults is demonstrated in Table 3. Compared with low urbanized group, the prevalence of HUA in medium and highly urbanized groups showed significant difference in univariate analysis, as shown in Table 1. Even after adjusting by age, gender, cardiometabolic risk factors, and health-related behaviors, the highly urbanized group still had higher risk of HUA compared with low urbanized group (OR 1.661, 95%CI 1.246-2.212, P=0.001). Furthermore, by subgroup analysis of the low and highly urbanized, age, gender, comorbidities (such as hypertension, diabetes, obesity, and CKD), and physical activity were suggested to affect the association between urbanization and the risk of HUA (Figure 2). Young and middle-aged males living in the community with higher community-level urbanization index were prone to higher risk of HUA. Such association also existed in individuals without hypertension, diabetes, obesity, or CKD and individuals with less physical activity.

Discussion

In the current study, we found that individuals living in highly urbanized areas were prone to higher risk of HUA. The association between urbanicity and HUA remained after adjusting for age, gender, and cardiometabolic/health-related behavioral risk factors.

Several potential mechanisms could explain the associations between high urbanicity and HUA. High pollution levels are present in highly urbanized areas[41-43]. Previous studies had shown that air pollution in China is mainly caused by population aggregation, urbanization, industrial discharges, outside investment, vehicle exhausts, coal consumption, technological development and straw burning[44, 45].Air pollution was reportedly associated with lower eGFR and increased prevalence of CKD, thus increasing the risk of hyperuricemia[46]. Furthermore, previous studies have confirmed that the air pollution contained toxic organic agents including polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs), perfluorinated alkyl substances (PFASa), and dioxins, which can increase serum uric acid concentrations and the incidence of HUA[47]. Exposure to greater concentrations of long-term ambient air pollutants has been confirmed to be associated with a higher incidence of hyperuricemia[14].

High urbanicity is accompanied with less physical activity. As found in our study, physical activity declined with the increase of urbanicity. In highly urbanized areas, occupational physical activity is less common, as well as the transportation and domestic activity, due to the popularity of motorized transportation and household appliances[48]. Physical exercise is closely associated with serum uric acid, as levels within professional endurance athletes are significantly lower than non-athletes[49]. After aerobic exercise, serum uric acid increases immediately and then decreases to a level even lower than pre-exercise level as energy-rich purine phosphates are transiently accumulated and catabolized, followed by the lasting-long depletion[50],. In our study, inadequate physical activity in individuals living in more urbanized communities increase the risk of HUA.

High urbanicity is associated with decreased kidney function. A previous study which included a large population revealed the higher risk of CKD in the higher urbanicity community[51]. As demonstrated in Table 1, the highly urbanized group had the highest prevalence of CKD. Kidney function is responsible for uric acid excretion and SUA, which was consistent with Table 2. The serum uric acid level of patients with CKD was higher than those without CKD.

Urbanization has associations with other non-communicable diseases, such as diabetes, hypertension, high LDL-c, cardiovascular disease, cancer, and neuropsychiatric disorders resulting from the changes in human activity, diet, and social structures in China[13]. These diseases can also increase the risk of HUA [1, 7, 11, 52].

In addition, we also found that age, gender, comorbidity (such as hypertension, diabetes, obesity, and CKD), and physical activity affect the association between urbanization and the risk of HUA. Young and middle-aged men living in the community with high community-level urbanization index are prone to higher risk of HUA. Such association also exists in individuals without hypertension, diabetes, obesity, and CKD and in individuals with less physical activity, suggesting that in more urbanized areas, individuals without traditional risk factors still have higher risk of HUA. The interaction between urbanicity and hypertension, diabetes, obesity, and CKD might conceal the relationship between urbanicity and HUA in these subgroups.

A strength of our study is that the CHNS data we analyzed in our survey is widely representative of the entire Chinese mainland. In addition, the innovative grouping and stratifying methods make it clear to distinguish the exact stage in which urbanicity exerts influences on HUA.

Our study also has some limitations. First, elderly individuals in our study tend to have lower serum uric acid. Reduced kidney function, hypertension, and diabetes can increase the risk of HUA and are common in elderly individuals. However, elderly individuals usually consume lower purine diets and pay more attention to health-related diets and behaviors compared to younger individuals. Effective diet control can reduce serum uric acid by 60~70μmol/L, which can partially explain the relationship between age and serum uric acid. Second, the association between urbanicity and HUA only exists in men after adjusting cardiometabolic and health-related behavioral risk factors. Females tend to smoke less, drink less, and be more inactive compared with males, thus their uric acid level is less influenced by urbanicity. Third, the association in the female group could be unavoidably affected because a fair amount of smoking data was missing. Fourth, even with self-reported history and physical and laboratory examination, the real prevalence of hypertension and diabetes mellitus might be under-reported. Finally, the population we analyzed was derived from China, and global data is needed to generalize the result.

In conclusion, living in highly urbanized areas is linked with higher risk of hyperuricemia independent of health-related behavioral and cardiometabolic risk factors, especially in individuals without traditional HUA risk factors such as hypertension, diabetes mellitus, obesity, and CKD.

Acknowledgements

We would like to acknowledge the team of the National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention, the Carolina Population Center, University of North Carolina at Chapel Hill, and the China–Japan Friendship Hospital, Ministry of Health who conducted the China Health and Nutrition Survey 2009. And we also acknowledge all the participants included in this study.

Ethics

The CHNS was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill, the China-Japan Friendship Hospital and the Chinese Center for Disease Control and Prevention's National Institute for

Nutrition and Health. All subjects gave informed consent for participation. The access to the data with approved by the above Institutional Review Board. The analysis of the data presented in this paper was approved by the Ethics Committee of Zhongshan Hospital, Fudan University (B2018-166).

Patient and Public Involvement statement

Patients and public had not been involved in the development of the research question or in the design of the study. Patients had received oral and written information about this research; however, they were not involved in the recruitment and conduct of the study. After signing informed consent, they were assessed for eligibility, and data collection began. Dissemination of the general results (no personal data) were approved only after the CHNS Review Board qualified the application.

Contributors

Zhang Xiaoyan and Ding Xiaoqiang were co-investigators and supervisors of the study. Yu Xixi carried out the study design, the data analysis and paper writing. Zhu Cheng provided the original idea of the paper, the original writing idea of the paper and played a vital role in revised submission. Zhang Han and Chen Jing served as scientific advisors and supervised data analysis. Shen Ziyan and Gu Yulu polished the article. Lv Shiqi, Zhang Di and Wang Yulin collected the data. All authors were involved in writing the paper and had final approval of the submitted and published versions.

Data sharing statement.

The datasets analyzed in the current study are available online (https://www.cpc.unc.edu/projects/china).

Competing Interests: None declared.

Funding

This study was supported by research grants from the Ministry of Science and Technology of People's Republic of China (2016YFC1305500), Shanghai Municipal Health Commission (2017ZZ01015), and the China National Natural Scientific Foundation (81700646 and 81970637). The funders had no roles in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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Table 1 Basic characteristics of participants according to community-level urbanization index

Variables	Low urbanized	Medium urbanized	Highly urbanized	*P* value
Number	3554	2162	2863	
SUA, mean (*SD*), μmol/L	5.02(1.69)	5.16(1.75)	5.42(1.87)	<0.001
HUA, *n (%)*	435(12.2)	316(14.6)	567(19.8)	<0.001
Age, mean (*SD*), year	50.29(14.76)	50.50(14.94)	52.15(15.37)	<0.001
Male, *n (%)*	1696(47.7)	1020(47.2)	1326(46.3)	0.549
Hypertension, *n (%)*	1169(32.9)	753(34.8)	1069(37.3)	0.001
DM, *n (%)*	296(8.3)	258(11.9)	374(13.1)	<0.001
High LDL-c, *n (%)*	1209(34.6)	1000(46.3)	1261(44.0)	<0.001
Obesity, *n (%)*	298(8.4)	212(9.8)	312(10.9)	<0.001
eGFR, mean (*SD*), mL/min per 1.73 m^2	81.98(16.46)	78.71(16.88)	76.57(16.94)	<0.001
CKD, *n (%)*	307(8.6)	255(11.8)	437(15.3)	<0.001
Smoking, *n (%)*	1108(31.2)	558(25.8)	708(24.7)	<0.001
Drinking, *n (%)*	791(22.3)	458(21.2)	536(18.7)	<0.001
Physical activity, mean (*SD*), METs	125.48(123.73)	81.53(101.49)	51.71(72.26)	<0.001

Continuous variables were expressed as the mean ± SD and categorical variables were described as frequencies and percentages. The one-way ANOVA test (for continuous variables) and χ2 tests (for categorical variables) were used to compare the difference between different group. SUA, serum uric acid; HUA: hyperuricemia; DM, Diabetes mellitus; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate; CKD chronic kidney disease; MET, metabolic equivalent for task.

Table 2 Factors associated with serum uric acid among Chinese adults.

	Univariable		Multivariable	
	β coefficient	***P* value**	**β coefficient**	**Adjusted *P* value**
Age (every 10 years)	0.019	<0.001	-0.028	<0.001
Gender (male *vs.* female)	0.287	<0.001	0.290	<0.001
Hypertension (yes *vs.* no)	0.110	<0.001	0.047	<0.001
DM (yes *vs.* no)	0.124	<0.001	0.067	<0.001
High LDL-c (yes *vs.* no)	0.031	<0.001	0.004	0.743
Obesity (yes *vs.* no)	0.133	<0.001	0.089	<0.001
CKD (yes *vs.* no)	0.195	<0.001	0.198	<0.001
Smoking (yes *vs.* no)	-0.018	0.307	-	-
Drinking (yes *vs.* no)	0.063	<0.001	0.037	0.001
Physical activity (every 10 METs)	<0.001	0.700	-	-
Community-level urbanization index (every 10 points)	0.016	<0.001	0.016	<0.001

The β coefficients and P values are from univariable and multivariable linear regression models of natural log-transformed uric acid as the dependent variable. The multivariable model included all covariates.DM, diabetes mellitus; LDL-c, low-density lipoprotein cholesterol; CKD, chronic kidney disease; MET, metabolic equivalent for task; –, without significance.

Table 3 Association of urbanization and the risk of hyperuricemia among Chinese adults

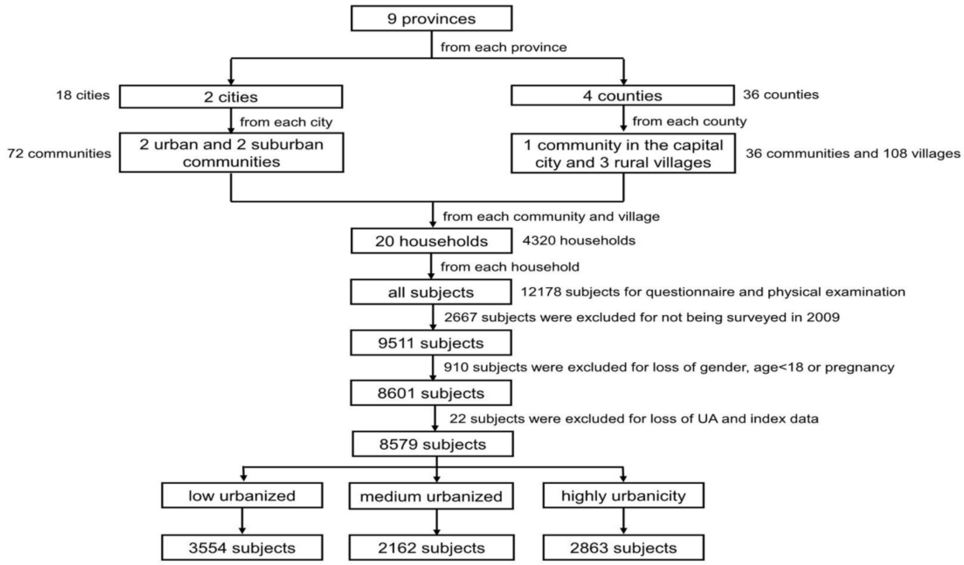
Variables	Low urbanized	Medium urbanized	Highly urbanized
hyperuricemia (%)	12.2	14.6	19.8
P[1]		0.009	<0.001
Odds ratio (95% CI)[1]	Ref.	1.234(1.055-1.445)	1.767(1.539-2.028)
P[2]		0.218	<0.001
Odds ratio (95% CI)[2]	Ref.	1.109(0.941-1.308)	1.548(1.339-1.789)
P[3]		0.363	0.001
Odds ratio (95% CI)[3]	Ref.	1.160(0.842-1.599)	1.661(1.246-2.212)

[1]Model 1 was only controlled by age, gender.[2]Model 2 was controlled by hypertension, diabetes mellitus and high low-density lipoprotein, obesity and chronic kidney disease based on Model 1.[3]Model 3 was controlled by health-related behaviors (smoking, drinking, physical activity) based on Model 2.

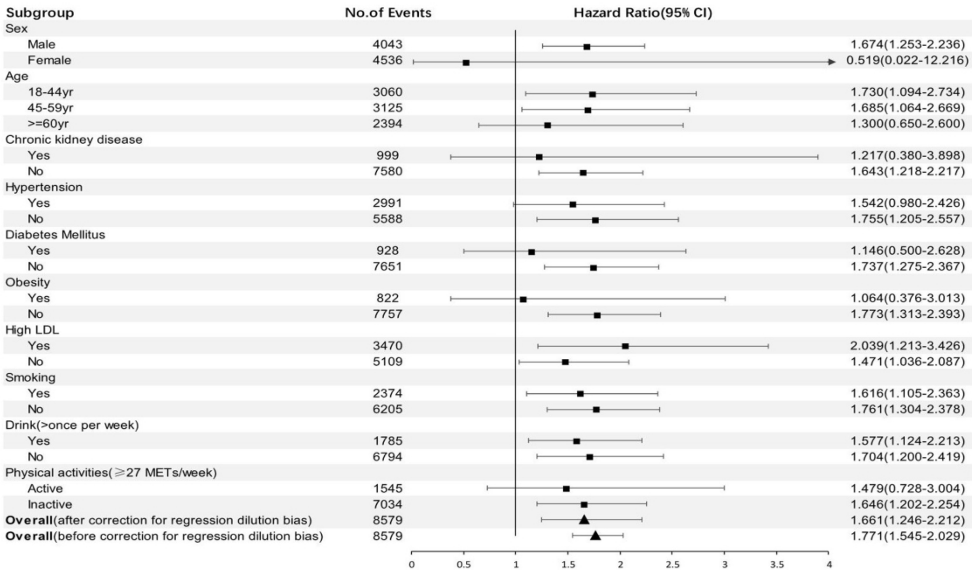
Figure Legend

Figure1 Flowchart of the sample selecting methods at each step.

Figure2 Adjusted odds ratios for hyperuricemia with high urbanicity according to baseline characteristics. Analyses were adjusted for age, gender, hypertension, diabetes mellitus, high LDL (high low-density lipoprotein), obesity, chronic kidney disease, smoking, drinking and physical activity, as appropriate. The square black boxes represent odds ratios, and the horizontal lines represent 95% confidence intervals. The triangle black boxes represent the overall odds ratios and 95% confidence intervals



Flowchart of the sample selecting methods at each step



Adjusted odds ratios for hyperuricemia with high urbanicity according to baseline characteristics.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5-6
Methods			
Study design	4	Present key elements of study design early in the paper	6-11
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6-7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9-11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-11
Bias	9	Describe any efforts to address potential sources of bias	11
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-11
		(*b*) Describe any methods used to examine subgroups and interactions	11
		(*c*) Explain how missing data were addressed	11
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	11
		(*e*) Describe any sensitivity analyses	11
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6-7
		(b) Give reasons for non-participation at each stage	6-7
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12
		(b) Indicate number of participants with missing data for each variable of interest	7
Outcome data	15*	Report numbers of outcome events or summary measures	12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-13

		(*b*) Report category boundaries when continuous variables were categorized	12
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	13
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	16-17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.