

Association Between Serum Uric Acid And Major Chronic Diseases Among Centenarians In China: Based On The CHCCS Study

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Abstract

Introduction: This study aims to analyze the distribution of SUA level based on more than 1,000 centenarians and to explore the association with three common diseases including hypertension, diabetes and dyslipidemia.

Methods: All the 1002 centenarians from the CHCCS were included. Household survey was conducted.

Results: The mean SUA level of centenarians was $329.04 \pm 97.75 \mu\text{mol/L}$ and the prevalence of hyperuricemia in centenarians was 26.5%. There was no statistical difference in the distribution of SUA levels among centenarians with or without hypertension/diabetes. For dyslipidemia, there was an independent positive association. The risk of dyslipidemia among those with hyperuricemia were 1.646 (95%CI: 1.078-2.298) compared with those who didn't have hyperuricemia. By comparing different subtypes of dyslipidemia, hyperuricemia was positively associated with hypertriglyceridemia and low-density lipoprotein cholesterolemia, with the corresponding ORs of 2.553 (95%CI: 1.282-5.083) and 1.927 (95%CI: 1.273-2.917) respectively, while there was no statistically significant association with hypercholesterolemia 0.998 (95%CI: 0.574-1.732).

Conclusions: There was no relation between SUA with hypertension or diabetes, while there was independently and positively association with hypertriglyceridemia and low-density lipoprotein cholesterolemia. The health benefits of controlling SUA in centenarians still require evidence based on prospective studies.

Introduction

Serum uric acid (SUA) is an important index of renal function. It is the product of protein metabolism¹. The current physiological reference value of SUA was mainly from data about adults²⁻⁴. However, it is well known kidney function deteriorates with age. The renal function of centenarians is far worse than that of adults and young elderly. But there is little data on the mean level of SUA about this extremely survivors⁶. Whether it is the same as the general elderly, or as a template for healthy aging, which is worth discussing.

On the other hand, SUA is not only an indicator of renal function, but also an important risk factor for cardiovascular disease and metabolic diseases. Meta-analysis showed that SUA was a risk factor for hypertension, metabolic syndrome, and coronary heart diseases⁷⁻⁸. Therefore, SUA has become one of the indicators for early warning and intervention of major chronic diseases including cardiovascular diseases. However, the current evidence is mostly about adults, a small part was from younger elderly aged <80 years old. There was a lack of basic data for centenarians. Whether this trend still exists among centenarians is unknown. That is to say, in centenarians, whether SUA is still an important risk factor for major diseases and needs to be controlled, there is no sufficient evidence yet. So, this study used data from one of Asia's largest centenarian survey to analyze the distribution of SUA level based on more than

1,000 centenarians and to explore the association with three common diseases including hypertension, diabetes and dyslipidemia.

Research Design And Methods

Study population

All the subjects in this study were from CHCCS, and the detailed research design framework was shown in previous articles⁹. In brief, this was a full sample survey. Based on the demographic data of 18 cities of Hainan Province provided by the Civil Affairs Bureau, we included all the people aged 100 and over in the study. A total of 1002 centenarians were invited to the survey and include in the analysis.

Investigation method

Household survey was conducted. All the questions on the questionnaire were asked and recorded by trained investigators. Centenarians were asked to answer health-related questions themselves. For those who were unable to answer the questions, the caregivers or relatives should answer on their behalf. All investigators were medical staff from Hainan hospital of Chinese PLA general hospital and have received unified training. Unified questionnaires were used to collect detailed demographic characteristics, disease history, family history, and lifestyles. Measurement indicators include height (For those who have a pot, measure their length), weight, waist circumference (WC), and blood pressure. Elbow vein blood was taken at 7-8 a.m. (more than 8 hours of fasting), and sent to the biochemical division of Hainan hospital of Chinese PLA general hospital to test related biochemical index, including total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (FPG), albumin (ALB), serum uric acid (SUC), creatinine (Scr), blood urea nitrogen (BUN).

Definitions

Centenarians referred to those who have certainly reached the age of 100 years old at the survey. Age was calculated by the survey minus the birth date. Body mass index (BMI) was calculated as weight (in kilograms) divided by the square of height (in meters).

Hyperuricemia was defined as positive if SUA level ≥ 420 $\mu\text{mol/L}$ in men or ≥ 360 $\mu\text{mol/L}$ in women or previous diagnosed.

Abdominal obesity was defined as positive if WC ≥ 90 cm in men or WC ≥ 80 cm in women.

Blood pressure was classified into the following categories: normal blood pressure: no history of hypertension in the past and SBP < 120 and DBP < 80 mmHg; prehypertension: no history of hypertension in the past and 120 mmHg < SBP < 140 mmHg or 80 mmHg < DBP < 90 mmHg; Hypertension, previous diagnosis or SBP ≥ 140 mmHg or DBP ≥ 90 mmHg.

Blood glucose was classified into the following categories: normal blood glucose, no history of diabetes in the past and $FPG \geq 6.1$ mmol/L; Impaired fasting glucose (IFG), no history of diabetes in the past and $6.1 \text{ mmol/L} \leq FPG < 7.0$ mmol/L; Diabetes, previous diagnosis or $FPG \geq 7.0$ mmol/L.

Blood lipids was classified into the following categories: normal blood lipids, no history of dyslipidemia in the past and total cholesterol (TC) < 5.18 mmol/L, triglyceride (TG) < 1.70 mmol/L, high density lipoprotein cholesterol (HDL-C) ≥ 1.04 mmol/L, and low density lipoprotein cholesterol (LDL-C) < 3.37 mmol/L; elevated blood lipids: no history of dyslipidemia in the past and $5.18 \text{ mmol/L} \leq TC < 6.22$ mmol/L, $1.70 \text{ mmol/L} \leq TG < 2.26$ mmol/L, and $3.37 \text{ mmol/L} \leq LDL-C < 4.14$ mmol/L; dyslipidemia, previous diagnosis or $TC \geq 6.22$ mmol/L, or $TG \geq 2.26$ mmol/L, or $HDL-C < 1.04$ mmol/L, or $LDL-C \geq 4.14$ mmol/L. The subtypes of dyslipidemia were classified into the following categories: Hypercholesterolemia, $TC \geq 6.22$ mmol/L; Hypertriglyceridemia, $TG \geq 2.26$ mmol/L; Combined hyperlipidemia, $TC \geq 6.22$ mmol/L and $TG \geq 2.26$ mmol/L; low-density lipoprotein cholesterololemia, $HDL-C < 1.04$ mmol/L.

Patient and Public Involvement

All centenarians were from Hainan Province. The investigation group obtained the list of centenarians from the Civil Affairs Department, and conducted household survey on those who agreed to participate in the survey. Health related information of the centenarians were collected by face-to-face questionnaire. All the centenarians were told and aware of the design and purpose of the study and participated in the study after signing informed consent. The results of laboratory test and physical examination should be fed back to the elderly in time.

Statistical analysis

All the analysis was conducted in SPSS 20.0 (SPSS Inc., Chicago, IL). Mean \pm SD and n(%) were used for continuous and categorical variables. Variance analysis and chi-square test were used for comparisons among different groups. Pearson correlation coefficients were used to describe correlations between SUA levels and other variables. Multivariate logistic regression was used to calculate the odds ratio (OR) of SUA for related diseases. As the independent variable, SUA was included in the model as two forms: continuous value and binary variable (hyperuricemia). Three diseases were considered as dependent variables, including hypertension, diabetes and dyslipidemia. We also used pre-hypertension/hypertension, IFG/diabetes, elevated lipids/dyslipidemia as dependent variables for sensitivity analysis. Covariates including demographic sociological characteristics (gender, age, ethnicity, culture, marriage, and previous work type), lifestyle (smoking, drinking, physical exercise, and dietary habits), and abdominal obesity were included in the logistic regression model.

Results

The mean age was 102.77 ± 2.55 years, with 82.0% were female. WC, TG, and HDL-C were related with SUA levels ($p < 0.05$). Correspondingly, there were statistical differences with abdominal obesity and dyslipidemia prevalence (table 1).

Distribution of SUA levels and prevalence of hyperuricemia

The mean SUA level of centenarians was $329.04 \pm 97.75 \mu\text{mol/L}$. 45.7% of them were between 250-350 $\mu\text{mol/L}$ and 81.4% were between 200-450 $\mu\text{mol/L}$. Only 5.7% were under 200 $\mu\text{mol/L}$ and 11.0% were $>450 \mu\text{mol/L}$ (appendix table 1).

The mean SUA level was higher among male than that of female ($379.86 \pm 110.08 \mu\text{mol/L}$ vs. $317.91 \pm 9.19 \mu\text{mol/L}$, $p < 0.001$). Compared with different age groups, the mean SUA levels were basically the same for each 5 years' age group (100-104, 105-109, 110-). That is, there was no increasing or decreasing trend of SUA levels with age.

The prevalence of hyperuricemia in centenarians was 26.5%. Male had a relatively higher prevalence than that in female, although not statistically significant (30.0% vs. 25.8%, $p = 0.247$). Similarly, there was no age-related trend ($p = 0.361$). (table 2)

Correlation analysis of SUA levels and three common diseases

As can be seen from table 3, SUA level was positively correlated with Scr and BUN level, with the Pearson's correlation coefficients 0.528 and 0.389 respectively ($p < 0.05$). In addition, SUA level was positively correlated with obesity related indicators, including weight and WC, with the Pearson's correlation coefficients 0.228 and 0.188 respectively ($p < 0.05$). The Pearson's correlation coefficients of SUA with systolic blood pressure (SBP), diastolic blood pressure (DBP), blood glucose were -0.003, -0.056 and -0.001 respectively ($p > 0.05$). On the other hand, SUA level was related with blood lipid, including TG ($r = 0.119$, $p < 0.05$) and HDL-C ($r = -0.101$, $p < 0.05$), but not with TC ($r = -0.006$, $P = 0.847$) and LDL-C ($r = 0.027$, $p = 0.401$).

Association between SUA levels and three common diseases

There was no statistical difference in the distribution of SUA levels among centenarians with or without hypertension. The mean SUA level for the three groups (normal blood pressure, pre-hypertension and hypertension) were $335.30 \pm 91.33 \mu\text{mol/L}$, $321.53 \pm 87.46 \mu\text{mol/L}$ and $330.30 \pm 100.69 \mu\text{mol/L}$ ($p = 0.473$) respectively (appendix table 2). The situation was similar with diabetes. The mean SUA level for the three groups (normal blood glucose, IFG and diabetes) were $328.84 \pm 95.58 \mu\text{mol/L}$, $329.35 \pm 87.13 \mu\text{mol/L}$, $330.49 \pm 122.62 \mu\text{mol/L}$, ($p = 0.987$). There was statistical difference among different blood lipids groups. The mean SUA level for the three groups (normal blood lipids, elevated blood lipids and dyslipidemia) were $311.87 \pm 90.91 \mu\text{mol/L}$, $325.19 \pm 89.63 \mu\text{mol/L}$ and $357.2 \pm 116.92 \mu\text{mol/L}$, ($p < 0.001$) respectively.

Table 4 showed the result of multivariate logistic regression analysis of the association between SUA level and three common diseases. Hypertension, diabetes and dyslipidemia were used as dependent variables separately; SUA level was used as the independent variable; the related covariates including demographic variables, lifestyles, disease history were also adjusted included in the model. As can be seen from Table 4, SUA levels was not associated with hypertension, the ORs were 1.000 (95%CI: 0.999-1.002) and 1.221 (95%CI: 0.874-1.707) when the independent SUA levels as continuous variable and

dichotomous variable (hyperuricemia). Similarly, SUA levels was not associated with diabetes either, the ORs were 1.000 (95%CI: 0.998-1.002) and 1.290 (95%CI: 0.818-2.037) respectively. For dyslipidemia, there was an independent positive association. The risk of dyslipidemia among those with hyperuricemia were 1.646 (95%CI: 1.078-2.298) compared with those who didn't have hyperuricemia. By comparing different subtypes of dyslipidemia, hyperuricemia was positively associated with hypertriglyceridemia and low-density lipoprotein cholesterolemia, with the corresponding ORs of 2.553 (95%CI: 1.282-5.083) and 1.927 (95%CI: 1.273-2.917) respectively, while there was no statistically significant association with hypercholesterolemia 0.998 (95%CI: 0.574-1.732).

Discussion

This result based on CHCCS showed that the prevalence of hyperuricemia in centenarians was high, and it had independently and positively association with hypertriglyceridemia and low density lipoprotein cholesterolemia while no association with hypertension or diabetes.

SUA level was higher than that of adults and younger elderly. The prevalence of hyperuricemia was also at a high level among centenarians. Previous study based on 22983 Chinese adults based on Chinese Physiological Constant and Health Conditions Study showed that the average SUA level in Chinese population was 346.1 μ mol/L and 258.6 μ mol/L for males and females respectively. The prevalence of hyperuricemia was 13.0%, while the prevalence went up to 20.5% among elderly¹⁰. The study based on elderly from Beijing showed the mean SUA levels were 345.1 μ mol/L and 309.4 μ mol/L in male and female respectively, and the prevalence of hyperuricemia was 16.7%¹¹. The meta-analysis based on 38 studies showed that the prevalence of hyperuricemia in Chinese people was 13.3%. This study showed that the mean SUA level was 329.04 μ mol/L in centenarians, which was higher than previous studies based on adults or younger elderly¹². Male had slightly higher SUA levels than female, but there was no statistical difference, which was consistent with previous results¹³. Meta-analysis showed that the gender difference of hyperuricemia prevalence narrowed among people aged 50 and over¹². It's partly because that with the decrease of estrogen after menopause, female lose the protective effects.

There was no relation between SUA with hypertension or diabetes, which was inconsistent with previous studies based on adults or younger elderly. Meta-analysis based on 18 cohort studies with 55607 people showed that the risk of hypertension among hyperuricemia patients were 1.41(95%CI: 1.23-1.58)¹⁴. Another meta-analysis based on 16 cohort study with 61714 people showed that the risk of diabetes among hyperuricemia patients were 1.131(95%CI: 1.084-1.179)¹⁵. However, the above meta-studies only included data on adults and people less than 80, and lacked data on centenarians. The association between SUA and diabetes or hypertension tends to weaken with the increase of age. The results from the Project of Longevity and Aging in Dujiangyan study also showed that SUA was not directly associated with hypertension based on 870 nonagenarians/centenarians⁶. Results from Health Professionals Follow-Up Study also showed similar results based on elderly men aged 60-85¹⁶. These results were consistent with the conclusion of our study. On the other hand, this study showed that SUA was

independently and positively correlated with hypertriglyceridemia and low-density lipoprotein cholesterolemia. A 5-year cohort study of 6476 adults from Japan showed that the risk of low-density lipoprotein cholesterolemia for every 1 mg/dL increase in SUA level was 1.159 (95% CI: 1.009-1.331) in male and 1.215 (95% CI: 1.061-1.390) in female respectively¹⁷. Another study based on the results of 8-year follow-up of 4190 adults, the incidence of hypertriglyceridemia was 28.2%, 29.1%, 36.9% and 45.6% respectively with the quartile of SUA level¹⁸. Those results were consistent with this study, which was the first to analyze the association of SUA with dyslipidemia and its subtypes (including hypertriglyceridemia and low-density lipoprotein cholesterolemia) in centenarians. The results showed that there was a significant positive correlation between SUA and hypertriglyceridemia and low-density lipoprotein cholesterolemia.

Our study has several strengths. This is the largest centenarian study in Asia with good representativeness. Second, unlike other sociological surveys that focus on sociology and less focus on health-related issues, this CHCCS survey was conducted by professional medical staff, which provided reliable and sufficient medical information. Third, we analyzed the association between SUA with all three common chronic diseases at the same time, which may be helpful for the comparisons.

Also, this study had several limitations. First, this was a cross-sectional study with limited causal inference, and the strength of causal inference is low, which still needs to be verified by prospective research. Second, SUA was a one-time test, which may be affected by diet and other factors. Third, lack of information about drug use may have an impact on the outcome. But, according to the appendix table 3, there was less than 1/4 of the centenarians who were taking medicine. Fourth, there may be survivor bias; the centenarians surveyed were relatively healthy people, which may underestimate the risk.

Conclusion

In summary, the results based on CHCCS with the largest sample among centenarians showed that centenarians had higher SUA levels and higher hyperuricemia prevalence. There was no relation between SUA with hypertension or diabetes, while there was independently and positively association with hypertriglyceridemia and low-density lipoprotein cholesterolemia. The health benefits of controlling SUA in centenarians still require evidence based on prospective studies.

Abbreviations

ALB, albumin; BL, blood lipids; BMI, body mass index; BUN, serum urea nitrogen; CI, confidence interval; CHCCS, China Hainan Centenarian Cohort Study; DBP, diastolic blood pressure; FBG, fasting plasma glucose; HDL-C, high density lipoprotein cholesterol; IFG, impaired fasting glucose; LDL-C, low density lipoprotein cholesterol; OR, odds ratio; SBP, systolic blood pressure; Scr, serum creatinine; SUA, serum uric acid; TC, total cholesterol; TG, triglyceride;

Declarations

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Contributors

All authors were involved in the design of the study, statistical analysis, interpretation of the data, drafting of the manuscript.

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Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Competing interests

None declared.

Consent for publication

Not required.

Ethics approval

This study was approved by the Biomedical Ethics Committee of Chinese PLA general hospital, and written informed consent with signature or fingerprint was obtained from each respondent.

Data availability statement

The datasets used during the current study are available on reasonable request.

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Tables

Table1. General characteristics of centenarians

Characteristics	Hyperuricemia		p
	Yes	No	
mean±SD			
Age (yrs)	102.79±3.01	102.76±2.65	0.853
Weight(kg)	38.72±8.18	37.17±7.31	0.004
WC(cm)	77.01±8.95	74.53±8.74	<0.001
BMI(kg/m ²)	18.37±3.47	17.92±3.37	0.271
SBP(mmHg)	154.05±25.75	152.03±23.93	0.247
DBP(mmHg)	75.01±12.68	76.02±13.03	0.276
TC(mmol/l)	4.64±0.99	4.69±0.99	0.459
TG(mmol/l)	1.27±0.75	1.14±0.61	0.005
HDL-C(mmol/l)	1.39±0.43	1.45±0.37	0.041
LDL-C(mmol/l)	2.81±0.82	2.81±0.78	0.926
FPG(mmol/l)	5.18±1.46	5.10±1.44	0.466
ALB(g/L)	38.42±3.88	38.52±4.05	0.734
SUA(μmol/L)	450.04±76.59	285.31±60.69	<0.001
n(%)			
Gender			0.247
Male	54(30.0)	126(70.0)	
Female	212(25.8)	610(74.2)	
Nationality			0.330
Han	230(26.0)	653(74.0)	
Minority	36(30.3)	83(69.7)	
Marriage status			0.343
Widowed	217(26.0)	619(74.0)	
Married/divorced/others	49(29.5)	117(70.5)	
Education level			0.880
Illiteracy	241(26.3)	674(73.7)	
Primary school	19(28.4)	48(71.6)	

Middle school or above	6(30.0)	14(70.0)	
Work types			0.410
Mental work	8(34.8)	15(65.2)	
Light or moderate physical labor	148(27.6)	388(72.4)	
Heavy physical labor	110(24.8)	333(75.2)	
Smoking			0.665
Never smoking	236(26.3)	660(73.7)	
Ever or current smoking	30(28.3)	76(71.7)	
Alcohol drinking			0.086
Never alcohol drinking	213(25.5)	623(74.5)	
Ever or current alcohol drinking	53(31.9)	113(68.1)	
Vegetables(≥ 1 time/day)			0.641
Yes	236(26.8)	645(73.2)	
No	30(24.8)	91(75.2)	
Fruits(≥ 1 time/day)			0.335
Yes	41(29.9)	96(70.1)	
No	225(26.0)	640(74.0)	
Meat(≥ 1 time/day)			0.568
Yes	92(25.5)	269(74.5)	
No	174(27.1)	467(72.9)	
Fish(≥ 1 time/day)			0.397
Yes	81(24.8)	245(75.2)	
No	185(27.4)	491(72.6)	
Eggs(≥ 1 time/day)			0.054
Yes	26(27.4)	69(72.6)	
No	250(27.6)	657(72.4)	
Milk(≥ 1 time/day)			0.774
Yes	31(27.7)	81(72.3)	
No	235(26.4)	655(73.6)	

Abdominal obesity			0.002
Yes	81(34.2)	156(65.8)	
No	185(24.2)	580(75.8)	
Hypertension			0.222
Yes	206(27.5)	542(72.5)	
No	60(23.6)	194(76.4)	
Dyslipidemia			0.001
Yes	72(35.6)	130(64.4)	
No	194(24.3)	606(75.8)	
Diabetes			0.272
Yes	30(31.3)	66(68.8)	
No	236(26.0)	670(74.0)	

Table 2. Distribution of SUA levels and hyperuricemia prevalence

	Male	Female	p	Total
SUA($\mu\text{mol/L}$)				
Age groups				
100-104 yrs	379.18 \pm 113.48	319.29 \pm 89.34	<0.001	330.59 \pm 97.16
105-109 yrs	383.27 \pm 92.75	311.11 \pm 100.28	<0.001	323.41 \pm 102.46
\geq 110 yrs	—	321.39 \pm 85.96		321.39 \pm 85.96
P	0.853	0.606		0.615
Total	379.86 \pm 110.08	317.91 \pm 91.19		329.04 \pm 97.75
Hyperuricemia [n(%)]				
Age groups				
100-104 yrs	42(28.0)	170(26.4)	0.682	212(26.7)
105-109 yrs	12(40.0)	31(21.2)	0.059	43(24.4)
\geq 110 yrs	—	11(35.5)	—	11(35.5)
P	0.190	0.356		0.361
Total	54(30.0)	212(25.8)	0.247	266(26.5)

Table3. Correlation analysis

Vararibles	r	p
Age (yrs)	-0.020	0.529
Weight(kg)	0.228	<0.001
WC(cm)	0.188	<0.001
BMI(kg/m ²)	0.114	<0.001
SBP(mmHg)	-0.003	0.918
DBP(mmHg)	-0.056	0.076
TC(mmol/l)	-0.006	0.847
TG(mmol/l)	0.119	<0.001
HDL-C(mmol/l)	-0.101	<0.001
LDL-C(mmol/l)	0.027	0.401
FPG(mmol/l)	-0.001	0.967
ALB(g/L)	0.048	0.132

Table 4. Multivariate analysis of SUA Level and major chronic diseases

Independent variables	SUA level (continuous, per $\mu\text{mol/L}$)		hyperuricemia(dichotomous)	
	OR(95%CI)	p	OR(95%CI)	p
Hypertension	1.000(0.999-1.002)	0.286	1.221(0.874-1.707)	0.242
Prehypertension & hypertension	1.000(0.997-1.002)	0.578	1.115(0.650-1.912)	0.691
Diabetes	1.000(0.998-1.002)	0.879	1.290(0.818-2.037)	0.273
IFG& diabetes	1.000(0.998-1.002)	0.995	1.255(0.878-1.793)	0.213
Dyslipidemia	1.003(1.002-1.005)	<0.001	1.646(1.078-2.298)	0.003
Elevated BL& Dyslipidemia	1.001(1.000-1.002)	0.142	1.201(1.001-1.594)	0.024
Hypercholesterolemia	1.001(0.999-1.004)	0.222	0.998(0.574-1.732)	0.993
Hypertriglyceridemia	1.005(1.002-1.008)	0.001	2.553(1.282-5.083)	0.008
Combined hyperlipidemia	1.007(1.002-1.011)	0.005	2.794(0.694-11.252)	0.148
Low HDL-C	1.004(1.002-1.006)	<0.001	1.927(1.273-2.917)	0.002

Adjusted for age, gender, nationality, education, marital status, BMI, work types, smoking, alcohol drinking, eating habits (vegetables, fruits, meat, fish, milk), abdominal obesity

Supplementary Files

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- [Appendixtables.docx](#)