BMJ Open Hyperuricaemia and associated factors among the oldest-old population in the urban areas of Chengdu, China: a community-based cross-sectional study

Xiang-Ji Chen,¹ Wenqiang Zhang,² Rui-Li Yuan,³ Xiao-Bo Huang ,⁴ Ya Liu,⁵ Rong-Hua Xu,⁶ Dong Wei,⁵ Wei-Wei Tang⁷

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X-JC and WZ contributed equally.

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For numbered affiliations see end of article.

Correspondence to

Dr Xiao-Bo Huang;
drxiaobo@163.com and
Dr Wei-Wei Tang;
homertang@njmu.edu.cn

ABSTRACT

Objectives To investigate the prevalence of hyperuricaemia among the oldest-old persons in Chengdu and identify associated factors to provide information on achieving healthy ageing in China.

Design

A community-based cross-sectional study.

Setting Jinjiang, Qingyang, Longquanyi locating in the southeast, the northwest and the east of Chengdu, respectively, were chosen as the study sites.

Participants A representative sample of 1391 people aged over 80 years were enrolled from September 2015 to June 2016, and 106 participants were excluded due to missing information. Thus, a total of 1285 participants were analysed in this study.

Outcome measures Hyperuricaemia was defined as serum uric acid >420 µmol/L in men or serum uric acid >360 µmol/L in women. A univariable logistic regression model and a multivariable logistic regression model were used to estimate the ORs and 95% CI to explore the associated risk factors of hyperuricaemia. **Results** The overall prevalence of hyperuricaemia among the oldest-old was 29.6%. There was no significant sex difference in the prevalence of hyperuricaemia, 29.1% in men vs 30.0% in women ($p>0.05$). Hyperlipidaemia and overweight were associated with the risk of hyperuricaemia both in men (OR 1.86; 95% CI 1.27 to 2.72; OR 2.44; 95% CI 1.42 to 4.19) and in women (OR 1.78; 95% CI 1.23 to 2.58; OR 2.95; 95% CI 1.89 to 4.61). Additionally, diabetes mellitus was associated with an increased prevalence of hyperuricaemia only in women (OR 1.99; 95% CI: 1.34 to 2.97).

Conclusion The burden of hyperuricaemia is substantial among the oldest-old population in the urban areas of Chengdu, China.

INTRODUCTION

Population ageing is a common phenomenon in the world.¹ Globally, the number of the oldest-old persons (aged 80 years or over² is projected to triple between 2019 and 2050, growing from 143 million to 426 million.¹ In China, the number of the oldest-old persons will increase more than fourfold between

Strengths and limitations of this study

- Evaluating the prevalence of hyperuricaemia among the oldest-old persons in Southwestern China can provide information on achieving healthy ageing in China.
- Guided by the recently proposed definition of hyperuricaemia addressing the subject of the negative impact of serum uric acid on the cardiovascular system, a 5.6 mg/dL cut-off was adopted to define hyperuricaemia and compared with the classic cut-off, which may provide reference for future hyperuricaemia-related studies.
- The rural setting of the study may compromise the representativeness of the sample.

2019 and 2050, growing from 26.1 million to reach 115.3 million, projected by the Population Division of the Department of Economic and Social Affairs of the United Nations.³ Healthy ageing is an imperative strategy to deal with population ageing.

Hyperuricaemia is a metabolic disease due to the overproduction or underexcretion of uric acid (UA), a natural product generated from the purine metabolism.^{4 5} The burden of hyperuricaemia is substantial both in developing and developed countries. The 2015–2016 National Health and Nutrition Examination Survey found that the prevalence of hyperuricaemia in the USA was 20.1%, approximately 47.13 million adults with hyperuricaemia.⁶ Data from the National Kidney Disease Surveillance Programme indicated that the prevalence of hyperuricaemia in the Irish was 24.5% in 2014, a pattern of increasing prevalence from 2006 to 2014.⁷ In the 2009–2010, China National Survey of Chronic Kidney Disease, the prevalence of hyperuricaemia was 8.4%, corresponding to a total of 92.9 million adults affected.⁸ Furthermore, the prevalence of hyperuricaemia

increased with advancing age, and the highest prevalence was observed in the oldest-old persons.^{6 7}

Thus, it is extremely significant to explore the prevalence of hyperuricaemia and associated factors in the oldest-old population. Although previous studies have reported that elevated serum UA (SUA) or hyperuricaemia is positively associated with atrial fibrillation,⁹ vascular inflammation,¹⁰ coronary artery disease,¹¹ better muscle function¹² in the oldest-old population, less evidence on the prevalence of hyperuricaemia among the oldest-old persons in China is known, with only one including 966 centenarians and 788 near-centenarians in the China Hainan Centenarian Cohort Study.¹³ Therefore, we conducted a community-based cross-sectional study to investigate the prevalence of hyperuricaemia among the oldest-old persons in Chengdu and identify associated factors to provide information on achieving healthy ageing in China.

METHODS

Study area

Chengdu is the capital city of Sichuan province, located at 30°05′—31°26′ N and 102°54′—104°53′ E. Chengdu is the fourth-largest city in China, the very centre of commerce, logistics, finance and science and technology, and the hub of transport and communication in Western China. The regional gross domestic product (GDP) of the city achieved 1701.265 billion in 2019, with an increase of 7.8%. The total resident population is more than 16 million in 2019, one of the most densely populated cities in China. Jinjiang, Qingyang, Longquanyi is located in the southeast, the northwest, and the east of Chengdu, respectively, which can be representative of the urban areas in Chengdu.

Participants

As described in detail previously,¹⁴ a community-based cross-sectional study was conducted in urban areas of Chengdu, China, from September 2015 to June 2016. Survey participants were randomly recruited using a multistage stratified cluster sampling method.¹⁴ A representative sample of 1391 people aged over 80 years were enrolled from three districts: Jinjiang, Qingyang, Longquanyi (figure 1). A total of 145 participants were excluded due to unwillingness, severe neurological and psychological diseases, including Alzheimer's disease, renal failure, end-stage cancer and severe frailty. This study consisted of three sections: a structured questionnaire, anthropometric measurements and laboratory tests. We excluded participants who had missing demographic information or fasting blood glucose, lipids and so on (n=65), and those whose SUA concentrations were missing (n=41). Subsequently, a total of 1285 participants were analysed in this study. Written informed consent was obtained from all subjects.

Data collection

As described in detail previously,¹⁴ data collection was completed by more than 20 trained medical staff in this

study. Demographic factors (eg, age and sex), health-risky behaviours (eg, smoking and drinking) and personal medical history (eg, the doctor's diagnosis or medication of hypertension) were collected using a self-reported questionnaire. Anthropometric data, blood pressure, blood biomarkers were collected using the standard examination. Body mass index (BMI, kg/m²) was calculated as weight (kg) divided by height (m) squared. Blood pressure was measured three times using standardised mercury sphygmomanometers. Using venous blood samples, total cholesterol (TC), triglycerides (TG) were measured by oxidase method, and blood glucose was measured by glucose oxidase method, and UA was measured by the phosphotungstic acid method in the Clinical Laboratory Center of the Second People's Hospital of Chengdu.

Variable measure

Smoking status and drinking status were clarified as 'never' or 'former and current'. Due to changes in body composition with ageing, overweight was defined as BMI >27 kg/m², acclaimed for the elderly (≥60 years).¹⁵ Hyperuricaemia was defined as SUA >420 µmol/L in men or SUA >360 µmol/L in women, according to Dietary guide for hyperuricaemia and gout patients (Chinese standard, WS/T 560–2017). Recent evidence suggested 5 mg/dL (333 µmol/L) was a more appropriate cut-off of SUA when investigating the negative impact of SUA on the cardiovascular system.¹⁶ For a comparison, hyperuricaemia was also defined as SUA >333 µmol/L (5.6 mg/dL) for both males and females. Hypertension was defined as systolic blood pressure (SBP) ≥140 mm Hg and (or) diastolic blood pressure (DBP) ≥90 mm Hg or the self-reported history or medication of hypertension. Diabetes was defined as fasting blood glucose ≥7.0 mmol/L and (or) oral glucose tolerance test (OGTT) 2-hour post-load glucose ≥11.1 mmol/L or the self-reported history or medication of diabetes. Dyslipidaemia was defined as TC ≥6.2 mmol/L, and/or low-density lipoprotein cholesterol (LDL-C) ≥4.1 mmol/L, and/or high-density lipoprotein cholesterol (HDL-C) <1.0 mmol/L, and/or TG ≥2.3 mmol/L, and/or the self-reported history or medication of dyslipidaemia, based on the Chinese guidelines for the management of dyslipidaemia in adults.¹⁷ History of kidney disease was defined as the self-reported of the doctor's diagnosis of kidney disease, including glomerulonephritis, pyelonephritis, hypertensive nephropathy, diabetic nephropathy, obstructive nephropathy, drug-induced nephropathy. A summary table was reported in online supplemental table 1.

Statistical analysis

All statistical analyses were performed while using Statistical Product and Service Solutions (SPSS, V.23.0). Categorical variables, including sex, smoking, drinking, hypertension, diabetes mellitus, dyslipidaemia and kidney disease, were presented as absolute numbers with the percentage, and Pearson's χ^2 test was used to detect

*Exclusion criteria refer to Methods section 2.2.

Figure 1 Flow chart on the sample selection and exclusion.

the difference between the sexes. Except for age and TG, continuous variables, including BMI, SBP, DBP, fasting plasma glucose (FPG), 2-hour plasma glucose (2hPG), TC, LDL-C, HDL-C, SUA, were presented as means with the SD, and Student's *t* test was used to detect the difference between the sexes. Age and TG were presented as medians with the IQR because of its skewed distribution, and the Wilcoxon's rank sum test was used to detect the difference between the sexes. Besides, stratified by sex, one-way analysis of variance (ANOVA) was used to detect the difference in SUA level between the age bands, and the Cochran-Armitage test was used to test the trend in hyperuricaemia prevalence between the age bands. A univariable logistic regression model and a multivariable logistic regression model were used to estimate the ORs and 95% CI to explore the associated risk factors of hyperuricaemia, using a forward-stepwise selection method (likelihood ratio) to specify how independent variables

are entered into the model. Values of $p < 0.05$ were considered to be statistically significant.

Patient and public involvement

No patient involved.

RESULTS

Participant characteristics

Table 1 shows the general and clinical characteristics of the study participants. The median age was 83 years in the total, in men, and in women. Men had higher prevalence rates of smoking and drinking than women ($p < 0.001$). The prevalence of diabetes mellitus was significantly higher in men than in women ($p = 0.015$), while there was no sex difference in the prevalence of hypertension, hyperlipidaemia, and kidney disease ($p > 0.05$). The BMI was significantly higher in men than in women ($p = 0.025$).

Table 1 General and clinical characteristics of the study participants

	Overall (n=1285)	Male (n=626)	Female (n=659)	P value
Age (years)	83 (81–86)	83 (81–86)	83 (81–85)	0.217
Former or current smoking	370 (28.8%)	279 (44.6%)	91 (13.8%)	<0.001
Former or current drinking	214 (16.7%)	180 (28.8%)	34 (5.2%)	<0.001
Hypertension	940 (73.2%)	457 (73.0%)	483 (73.3%)	0.841
Diabetes mellitus	350 (27.2%)	190 (30.4%)	160 (24.3%)	0.015
Hyperlipidaemia	378 (29.4%)	171 (27.3%)	207 (31.4%)	0.107
Kidney disease	31 (2.4%)	13 (2.1%)	18 (2.7%)	0.445
BMI (kg/m ²)	23.0±3.9	23.3±3.6	22.8±4.1	0.025
SBP (mm Hg)	149.5±21.7	147.4±20.1	151.5±22.9	0.001
DBP (mm Hg)	74.1±12.0	74.5±11.3	73.7±12.6	0.279
FPG (mmol/L)	5.6±2.1	5.7±2.2	5.5±2.0	0.092
2hPG (mmol/L)	8.6±3.7	8.7±2.7	8.4±4.4	0.260
TG (mmol/L)	1.21 (0.91–1.64)	1.15 (0.85–1.64)	1.25 (0.95–1.70)	<0.001
TC (mmol/L)	4.81±0.92	4.57±0.85	5.04±0.93	<0.001
LDL-C (mmol/L)	2.61±0.75	2.47±0.71	2.74±0.76	<0.001
HDL-C (mmol/L)	1.62±0.42	1.54±0.41	1.70±0.43	<0.001
SUA (μmol/L)	334.6±117.7	360.0±118.3	310.4±111.9	<0.001

Data are presented as mean±SD, n (%); Age and TG were reported as median (IQR).

BMI, body mass index; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; 2hPG, 2-hour plasma glucose; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; SUA, serum uric acid; TC, total cholesterol; TG, triglyceride.

Men had lower SBP than women ($p=0.001$), although there was no sex difference in DBP ($p>0.05$). Moreover, there was no sex difference in the FPG level and 2hPG level ($p>0.05$). However, men had lower TG, TC, LDL-C, HDL-C than women ($p<0.001$). The SUA level was significantly higher in men than in women ($p<0.001$).

SUA level and hyperuricaemia

Men affected with hyperuricaemia ($484.4\pm71.1\mu\text{mol/L}$) had higher level of SUA than healthy men ($309.1\pm93.5\mu\text{mol/L}$, $p<0.001$), and women affected with hyperuricaemia ($424.4\pm61.9\mu\text{mol/L}$) had higher level of SUA than healthy women ($261.4\pm91.1\mu\text{mol/L}$, $p<0.001$). Figure 2A shows the age-specific SUA level. The mean SUA level in men was $357.8\mu\text{mol/L}$ (SD=110.9) for aged 80–84 years, $363.7\mu\text{mol/L}$ (SD=138.2) for

aged 85–89 years, $366.5\mu\text{mol/L}$ (SD=113.1) for aged 90–98 years, respectively. In women, the mean SUA level was $307.7\mu\text{mol/L}$ (SD=109.2) for aged 80–84 years, $312.9\mu\text{mol/L}$ (SD=117.9) for aged 85–89 years, $321.8\mu\text{mol/L}$ (SD=116.7) for aged 90–98 years, respectively. There was no statistical significance in the SUA level between the age bands among men and women ($p>0.05$). In addition, the prevalence of hyperuricaemia among the oldest-old was 29.6% in the total, 29.1% in men, 30.0% in women, respectively, and there was no sex difference ($p>0.05$). Figure 2B shows the age-specific prevalence of hyperuricaemia. Among men, 27.7% (114/412) of aged 80–84 years, 33.1% (52/157) of aged 85–89 years, 28.1% (16/57) of aged 90–98 years had hyperuricaemia. 27.7% (122/441) of aged 80–84 years, 36.9% (55/149) of aged 85–89 years, 30.4% (21/69) of aged 90–98 years had hyperuricaemia in women. There was no increasing trend of hyperuricaemia prevalence between the age bands ($p=0.483$ in men; $p=0.175$ in women). With a recently proposed definition of hyperuricaemia, the prevalence of hyperuricaemia among the oldest-old was 50.4% in the total, 62.6% in men, 38.8% in women, respectively, and men had a higher prevalence of hyperuricaemia than women ($p<0.001$). The prevalence of hyperuricaemia decreased with advanced age in men ($p=0.00025$, (online supplemental figure 1).

Figure 2 Age-specific serum uric acid level and prevalence of hyperuricaemia among the oldest-old in Southwestern China. (A) Age-specific serum uric acid level in males and females; (B) prevalence of hyperuricaemia in each age and gender group. ANOVA, analysis of variance.

Table 2 Comorbidities of hyperuricaemia among the study participants by sex

Comorbidity	Male		Female	
	Hyperuricaemia	Normal	Hyperuricaemia	Normal
Hypertension	142 (78.0)	315 (70.9)*	153 (77.3)	330 (71.6)
Diabetes mellitus	56 (30.8)	134 (30.2)	73 (36.9)	87 (18.9)*
Hyperlipidaemia	69 (37.9)	102 (23.0)*	82 (41.4)	125 (27.1)*
Overweight	31 (17.0)	32 (7.2)*	58 (29.3)	53 (11.5)*

Data are presented as n (%).

*P<0.05.

Comorbidities of hyperuricaemia

Among men affected with hyperuricaemia (table 2), 78.0%, 30.8%, 37.9%, 17.0% had hypertension, diabetes mellitus, hyperlipidaemia and overweight, respectively. Men affected with hyperuricaemia had higher prevalence of hypertension, hyperlipidaemia and overweight than the normal level of SUA ($p<0.05$). 77.3%, 36.9%, 41.4%, 29.3% of women with hyperuricaemia had hypertension, diabetes mellitus, hyperlipidaemia and overweight, respectively. Women affected with hyperuricaemia had a higher prevalence of diabetes mellitus, hyperlipidaemia and overweight than the normal level of SUA ($p<0.05$). With a recently proposed definition of hyperuricaemia, very similar results were reported in online supplemental table 2.

Associated factors of hyperuricaemia

Table 3 shows the ORs for hyperuricaemia using the univariable and multivariable logistic regression analyses. In the univariable logistic regression analysis (model 1), hypertension, hyperlipidaemia and overweight were positively associated with hyperuricaemia in men. Age,

diabetes mellitus, hyperlipidaemia and overweight were positively associated with hyperuricaemia in women. In the multivariable logistic regression analysis (model 2), hyperlipidaemia and overweight were positively associated with the risk of hyperuricaemia in men. Compared with participants aged 80–84 years, those aged 85–89 years had a higher risk of hyperuricaemia in women. Besides, diabetes mellitus, hyperlipidaemia and overweight were positively associated with the risk of hyperuricaemia in women. Logistic regression analyses using a recently proposed definition of hyperuricaemia delivered similar results (online supplemental table 3).

DISCUSSION

In this representative sample of the community-based population in Chengdu, we observed a substantial burden of hyperuricaemia in the urban oldest-old. Specifically, the overall prevalence of hyperuricaemia was 29.6%. There was no significant sex difference in the prevalence of hyperuricaemia, 29.1% in men vs 30.0% in women.

Table 3 ORs for hyperuricaemia among the study participants by sex

	Male		Female	
	Model 1	Model 2	Model 1	Model 2
Age groups				
80–84 years	1.00 (reference)	–	1.00 (reference)	1.00 (reference)
85–89 years	1.30 (0.87–1.92)	–	1.53 (1.03–2.27)*	1.80 (1.19–2.73)*
90–98 years	1.02 (0.55–1.89)	–	1.14 (0.66–1.99)	1.70 (0.94–3.07)
Former or current smoking	1.24 (0.88–1.75)	–	0.81 (0.49–1.34)	–
Former or current drinking	1.15 (0.79–1.67)	–	0.83 (0.38–1.81)	–
Hypertension	1.56 (1.03–2.36)†	–	1.29 (0.87–1.90)	–
Diabetes mellitus	1.03 (0.71–1.50)	–	2.51 (1.73–3.64)*	1.99 (1.34–2.97)*
Hyperlipidaemia	2.05 (1.41–2.97)†	1.86 (1.27–2.72)†	1.90 (1.34–2.70)*	1.78 (1.23–2.58)*
Kidney disease	2.92 (0.97–8.81)	–	1.17 (0.43–3.16)	–
Overweight	2.65 (1.56–4.50)†	2.44 (1.42–4.19)†	3.22 (2.11–4.90)*	2.95 (1.89–4.61)*

Data are presented as odds ratios (95% CI). Model 1 was a univariable logistic regression model. Model 2 was a multivariable logistic regression model, using a forward-stepwise selection method (likelihood ratio) to specify how independent variables are entered into the model.

*P<0.05.

†For missing values, we created a dump variable for missing values.

Using a recently proposed cut-off of SUA, identified as that above which cardiovascular mortality significantly,¹⁶ the prevalence of hyperuricaemia among the urban oldest-old population was 50.4%. Multivariable analyses found that hyperlipidaemia and overweight were associated with the risk of hyperuricaemia in the oldest-old population, regardless of sex. Furthermore, there was a significant association between diabetes mellitus and hyperuricaemia only in women, but not in men.

In this study, our estimated prevalence of hyperuricaemia among the oldest-old is approximate to the Chinese centenarians and near-centenarians (29.02%)¹³, remarkably more than that from adults aged 18 years and older in the 2009–2010 China National Survey of Chronic Kidney Disease (8.4%).⁸ It has been reported that the prevalence of hyperuricaemia is highest in the oldest-old population, 27.8% in the USA,⁶ 43.0% in the Irish.⁷ Differences in the prevalence of hyperuricaemia among the oldest-old may be accounted for the race, region, dietary habits.^{6 7 13} Higher Seafood consumption, higher meat consumption and lower vegetable consumption were significantly associated with the increasing risk of hyperuricaemia among the centenarians and near-centenarians.¹³

Of note, the prevalence of hyperuricaemia defined by a recently proposed cut-off of SUA (5.6mg/dL) was 70.3% higher than that in the classic definition (7.0mg/dL in men and 6.0mg/dL in women), consistent with a previous study.¹⁸ A 5.6mg/dL was identified as a higher risk of cardiovascular mortality among Italians,¹⁶ more multicentre and multiethnic prospective studies are needed to prove external validity in health outcomes.

Previous studies have shown the higher prevalence of hyperuricaemia among adults in men than in women.^{8 19–21} However, our study indicated no difference in the prevalence of hyperuricaemia among the oldest-old between men and women. Young women adults with a lower prevalence of hyperuricaemia can be explained by the uricosuric effects of oestrogen.^{22–24} Following menopause, the prevalence of hyperuricaemia rose sharply in older women.^{7 22 23} The effect of oestrogen disappeared in the oldest-old women, which may account for no sex difference in the prevalence of hyperuricaemia.

Our findings appear in agreement with a previous study in China, where the positive association between high TG and hyperuricaemia among the oldest-old was observed in both men and women.²⁵ Moreover, overweight was positively associated with the prevalence of hyperuricaemia in the oldest-old, consistent with a study among long-lived Chinese subjects aged 90 years and older, indicating that higher levels of SUA may be positively associated with higher BMI.²⁶ Besides, diabetes mellitus was associated with an increased prevalence of hyperuricaemia only in women. Nevertheless, evidence from observational studies can be biased by potential confounding factors and reverse causality. Thus, high-quality studies such as Mendelian randomisation studies should be carried out to confirm whether there is a causal association between

cardiovascular disease risk factors and hyperuricaemia in the oldest-old population.

Our studies have several limitations. First, the definition of hyperuricaemia merely relied on the concentration of SUA. Medication information (eg, diuretic)²⁷ that may affect the level of SUA was not available, which can cause the estimated prevalence of hyperuricaemia subject to error. Second, potential confounding factors such as dietary intakes were not included. Third, kidney disease was defined by a self-reported history, rather than estimated glomerular filtration rate, which might cause a false-negative result.²⁸ Moreover, all participants were recruited from the urban oldest-old population, so the results may not be generalisable to the rural oldest-old population. Finally, the association observed in this study resulted from a cross-sectional study, which may suffer from potential biases and reverse causality. Thus, more prospective studies or Mendelian Randomisation studies are needed to determine causality. Notably, this is the first comprehensive study that accurately evaluated the prevalence of hyperuricaemia among the oldest-old persons in Southwestern China, and identified factors associated with hyperuricaemia.

In conclusion, this study demonstrated that the burden of hyperuricaemia is substantial among the oldest-old population in the urban areas of Chengdu, China. Hyperlipidaemia and overweight are associated with the increasing prevalence of hyperuricaemia in both sexes, but the association between diabetes mellitus and hyperuricaemia is observed only in women. Further studies should be carried out to confirm the causal association.

Author affiliations

¹Department of Geriatric Medicine, Inner Mongolia People's Hospital, Hohhot, Inner Mongolia, China

²Department of Epidemiology and Health Statistics, West China School of Public Health and West China Fourth Hospital, Sichuan University, Chengdu, Sichuan, China

³Department of Hematology and Rheumatology, Chengdu Second People's Hospital, Chengdu, Sichuan, China

⁴Department of Cardiology, Chengdu Second People's Hospital, Chengdu, Sichuan, China

⁵Department of Endocrinology and Metabolism, Chengdu Second People's Hospital, Chengdu, Sichuan, China

⁶Stroke Center, Chengdu Second People's Hospital, Chengdu, Sichuan, China

⁷School of Health Policy and Management, Nanjing Medical University, Nanjing, Jiangsu, China

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ORCID iD

Xiao-Bo Huang <http://orcid.org/0000-0002-4692-1433>

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