

Prevalence of and risk factors for high-altitude hyperuricaemia in Bai individuals: a cross-sectional study

Journal of International Medical Research

49(7) 1–11

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DOI: 10.1177/03000605211028140

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Abstract

Objective: Hyperuricaemia is common in Bai individuals; however, its prevalence remains unclear. This work aimed to investigate high-altitude hyperuricaemia prevalence and risk factors in Bai individuals.

Methods: All eligible participants of Bai ethnicity (aged ≥ 18 years and undergoing routine medical examination at the People's Hospital of Jianchuan County between January and December 2019) were consecutively enrolled. Demographic and laboratory data were collected to investigate hyperuricaemia prevalence and associated risk factors.

Results: A total of 1393 participants were assessed, comprising 345 (24.8%) with hyperuricaemia showing a male predominance (287/865 [33.2%] males versus 58/528 [11.0%] females). Hyperuricaemia prevalence was significantly higher in participants aged ≥ 50 years (100/332 [30.1%]) versus those aged 30–40 years (59/308 [19.2%]), and in overweight/obese individuals

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These data were presented in part at the 57th European Renal Association & European Dialysis and Transplant Association Congress, ERA-EDTA 2020, Milan, Italy, 6–9 June 2020; poster No. P0177: Gao C, Duan Y, Jia L, et al. P0177 Prevalence and risk factors of hyperuricemia in the Bai ethnic group in southwestern China. *Nephrology Dialysis Transplantation* 2020; 35, Supplement_3: gfaa142. P0177.

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compared with those showing an underweight or normal body mass index (BMI; 267/885 [30.2%] versus 78/508 [15.4%]). Finally, haemoglobin concentrations and serum uric acid levels were positively correlated.

Conclusion: Besides traditional risk factors, including age, sex and BMI, polycythaemia due to prolonged exposure to high altitude may also cause hyperuricaemia in Bai individuals residing in Yunnan Province.

Keywords

Hyperuricaemia, risk factors, prevalence, polycythaemia, haemoglobin, serum uric acid

Date received: 9 November 2020; accepted: 8 June 2021

Introduction

Remarkable progress has been made to reveal the associations between serum uric acid (SUA) levels and cardiovascular and renal diseases. Epidemiological evidence indicates associations between hyperuricaemia and elevated incidence rates of cardiovascular events and all-cause mortality in patients without pre-existing cardiovascular diseases.¹ Moreover, hyperuricaemia is an independent predictive factor of chronic kidney disease in subjects with normal renal function, including those with diabetes.² Thus, hyperuricaemia is considered to be one of the major chronic diseases threatening humans, as it increases the risk of many comorbidities and mortality.³

Hyperuricaemia is a national public health concern in China with consistently increasing prevalence. According to a meta-analysis including 44 studies, a pooled prevalence of 13.3% (95% confidence interval [CI] 11.9%, 14.6%) was obtained for hyperuricaemia, with prevalence rates of 5.5–23.5%.⁴ Significantly different prevalence rates were found in distinct geographical regions in China,⁵ and although prolonged exposure to high altitude may promote hyperuricaemia,⁶ the enrolled studies encompassed eastern areas with relatively low altitudes.⁵

The Bai ethnic population represents a well-known minority group in China,

totalling 1.93 million people, with more than 80% of individuals residing in the Dali Bai Autonomous Prefecture of Yunnan Province, Southwestern China. Hyperuricaemia prevalence in Bai individuals remains unknown. Thus, the aim of the current study was to assess epidemiological data related to hyperuricaemia in individuals of Bai ethnicity, to provide information for improving the health status of the Bai ethnic population.

Participants and methods

Study population

This retrospective cross-sectional study consecutively enrolled all eligible participants of Bai ethnicity, aged ≥ 18 years, who were undergoing routine medical examination at the People's Hospital of Jianchuan County (mean altitude approximately 2300 m) between January and December 2019. Pregnant women, and patients diagnosed with malignant tumours, mental health diseases, and/or severe heart, renal, or hepatic failure, according to medical records or self-reported diagnoses, were excluded from the study. Data regarding age, sex, height, weight, systolic and diastolic blood pressure (SBP and DBP, respectively), complete blood count (CBC), SUA, and serum urea, creatinine, fasting glucose, total protein, albumin, cholesterol

and triglyceride levels, were obtained. Each participant provided written informed consent and all participant details were de-identified. Due to the retrospective, cross-sectional design, the study received exemption from ethics board approval by the Ethics Committee of Ruijin Hospital, Shanghai Jiao Tong University, School of Medicine (Shanghai, China). The study conformed to STROBE guidelines for reporting observational studies.⁷

Clinical examination and laboratory measurements

Data were collected according to the medical examination system at the People's Hospital of Jianchuan County. Height and weight were measured twice in each participant, using an automatic HNH-219 height/weight measurement device (Omron, Kyoto, Japan) after removing shoes and heavy clothing, and the mean reading on a calibrated scale was recorded. BP was measured from the right arm with an automatic HBP-9020 sphygmomanometer (Omron), three times, at 2-min intervals following ≥ 5 min of rest. Mean SBP and DBP readings were then calculated. Venous blood samples (2 ml for CBC plus 3–4 ml for biochemical analysis) were obtained after overnight fasting by trained medical staff and analysed in the People's Hospital of Jianchuan County immediately upon delivery to the laboratory. CBCs were evaluated using an XS-1000i automated haematology analyser (SYSMEX; Kobe, Japan). Biochemical parameters, such as levels of SUA, and serum urea, creatinine, fasting glucose, total protein, albumin, cholesterol, triglyceride, and high- and low-density lipoprotein cholesterol (HDL-c and LDL-c, respectively) were assessed on a LABOSPECT 008 AS auto-analyser (Hitachi, Ibaraki Prefecture, Japan).

Definitions

Hypertension was defined as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg.⁸ Hyperuricaemia was defined as fasting SUA > 360 $\mu\text{mol/l}$ in females and > 420 $\mu\text{mol/l}$ in males.⁹ Body mass index (BMI) was derived by dividing the weight (kg) by the squared height (m). Participant grouping based on BMI was as follows:¹⁰ underweight, < 18.5 kg/m^2 ; normal weight, 18.5 – 22.9 kg/m^2 ; overweight, 23 – 27.4 kg/m^2 ; obese, ≥ 27.5 kg/m^2 . Polycythaemia was defined as increased haemoglobin concentration (> 165 g/l in males and > 160 g/l in females) and/or haematocrit ($> 49\%$ in males and $> 48\%$ in females) in peripheral blood.¹¹

Statistical analyses

Continuous and categorical variables are presented as mean \pm SD or number (percentage), respectively, and between-group differences were analysed by χ^2 -test (categorical data) and Student's *t*-test (continuous data). Associations between SUA levels and variables such as total cholesterol, triglyceride, HDL-c, LDL-C, fasting glucose, total protein, and albumin levels, were predicted by univariable correlation analysis. Multivariable logistic regression analysis was performed to determine risk factors for hyperuricaemia among parameters showing significance in univariable correlation analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were determined to quantify the associations. Data were analysed with SPSS software, version 22.0 (IBM, Armonk, NY, USA), and a *P* value < 0.05 indicated statistical significance.

Results

Baseline characteristics

A total of 1393 participants were assessed in this study, comprising 865 (62.1%) males

and 528 (37.9%) females. Baseline features were compared between the sexes and between those with or without hyperuricaemia (summarized in Table 1). Male participants were found to have significantly increased height, weight, BMI, SBP, DBP, SUA, and serum urea, creatinine, fasting glucose, total cholesterol, triglyceride, HDL-c, LDL-c, red blood cell (RBC), haemoglobin (Hb), and haematocrit (Hct) levels compared with female participants. Height, weight, BMI, SBP, DBP, SUA, serum urea, creatinine, total cholesterol, triglyceride, LDL-c, RBC and Hb were significantly higher in participants with hyperuricaemia compared with those without hyperuricaemia (all $P < 0.001$).

Hyperuricaemia rates in different sex and age groups

The overall hyperuricaemia prevalence was 24.8% (345/1393), of whom, 287 (83.2%) were male and 58 (16.8%) were female. The rate of hyperuricaemia was elevated in men compared with women (287/865 [33.2%] versus 58/528 [11.0%], $\chi^2 = 86.68$, $P < 0.001$). In order to assess the potential association between hyperuricaemia prevalence and age, participants were categorized into four groups: 268 participants (male/female, 147/121) aged ≤ 30 years; 308 (male/female, 159/149) aged 30–40 years; 485 (male/female, 294/191) aged 40–50 years; and 332 (male/female, 265/67) aged > 50 years. Hyperuricaemia rates in these age groups were 74 (27.6%), 59 (19.2%), 112 (23.1%), and 100 (30.1%), respectively, which formed a 'U' shaped distribution. The number and proportion of male participants with hyperuricaemia in each age group was 57 (38.8%), 52 (32.7%), 93 (31.6%), and 85 (39.5%), respectively, and the number and proportion of female participants with hyperuricaemia was 17 (14.0%), 7 (4.7%), 19 (9.9%), and 15 (22.4%), respectively. Of note,

hyperuricaemia rates in males were significantly elevated than those of females in all age groups ($P < 0.001$) except the group aged > 50 years (Figure 1). Furthermore, SUA levels were significantly elevated in males compared with females in the different age groups (Figure 1).

Hyperuricaemia and nutritional status

Univariable correlation analysis (Table 2) demonstrated that SUA was positively correlated with total cholesterol, triglyceride, and LDL-c levels in the all-participant group, and in males and females, respectively. SUA was inversely correlated with HDL-c in the all-participant group and in females. Multivariable logistic regression analysis (Table 3) revealed that total cholesterol (OR 1.409, 95% CI 1.280, 1.552) and LDL-c (OR 3.082, 95% CI 2.260, 4.204) levels were risk factors for hyperuricaemia in Bai individuals.

Based on BMI, 508, 675 and 210 individuals were classified in the underweight/normal, overweight and obesity groups, respectively. The numbers of participants with hyperuricaemia in the three groups were 78 (male/female, 60/18), 168 (male/female, 148/20), and 99 (male/female, 79/20), respectively, indicating prevalence rates of 15.4%, 24.9%, and 47.1%, respectively. These findings showed that hyperuricaemia prevalence increased with increasing BMI, and the overweight and obesity groups displayed markedly elevated SUA levels compared with individuals who were underweight or normal weight (Figure 2).

Hyperuricaemia and polycythaemia

The overall prevalence of polycythaemia was 51.5% (717/1393). In male and female participants, respectively, mean haematocrit levels were $49.75 \pm 3.56\%$ and $42.92 \pm 3.65\%$, and mean haemoglobin

Table 1. Demographic and laboratory characteristics in a Bai ethnic population.

Characteristic	Study group			
	Overall (n = 1393)	Male (n = 865)	Female (n = 528)	Non-hyperuricaemia (n = 1048)
Age	42.34 ± 11.67	44.02 ± 12.45	39.59 ± 9.65**	42.17 ± 11.39
Height, cm	163.62 ± 7.84	167.60 ± 6.23	157.11 ± 5.48**	162.69 ± 7.89**#
Weight, kg	65.22 ± 11.43	69.21 ± 10.71	58.70 ± 9.40**	63.13 ± 10.72**#
BMI, kg/m ²	24.28 ± 3.41	24.61 ± 3.39	23.75 ± 3.37**	23.78 ± 3.21**#
SBP, mmHg	121.40 ± 14.90	122.77 ± 14.78	119.15 ± 14.83**	120.12 ± 14.81**#
DBP, mmHg	76.37 ± 11.39	77.86 ± 11.53	73.92 ± 10.72**	75.39 ± 11.17**#
Urea, mmol/l	5.36 ± 1.56	5.64 ± 1.58	4.90 ± 1.41**	5.27 ± 1.55**#
Creatinine, μmol/l	69.77 ± 15.83	78.15 ± 13.04	56.05 ± 8.90**	67.04 ± 14.85**#
SUA, μmol/l	348.56 ± 90.85	390.95 ± 77.78	279.13 ± 64.06**	310.27 ± 63.34**#
Fasting glucose, mmol/l	5.17 ± 1.24	5.27 ± 1.39	5.00 ± 0.92**	5.15 ± 1.26
TC, mmol/l	5.30 ± 1.07	5.44 ± 1.09	5.06 ± 0.98**	5.20 ± 1.02**#
TG, mmol/l	1.73 ± 1.59	1.97 ± 1.79	1.34 ± 1.08**	1.56 ± 1.48**#
HDL-c, mmol/l	1.67 ± 0.34	1.63 ± 0.35	1.72 ± 0.32**	1.67 ± 0.34
LDL-c, mmol/l	3.07 ± 0.87	3.23 ± 0.88	2.81 ± 0.80**	2.97 ± 0.84**#
RBC, × 10 ⁹ /l	5.31 ± 0.61	5.58 ± 0.54	4.87 ± 0.43**	5.25 ± 0.62**#
Hb, g/l	163.11 ± 18.94	173.57 ± 13.24	145.97 ± 13.64**	160.76 ± 19.35**#
Hct, %	47.16 ± 4.89	49.75 ± 3.56	42.92 ± 3.65**	46.59 ± 4.99

Data presented as mean ± SD.

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; SUA, serum uric acid; TC, total cholesterol; TG, triglycerides; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; RBC, red blood cell; Hb, haemoglobin; Hct, haematocrit.

***P* < 0.001, versus male; ##*P* < 0.001, versus hyperuricaemia group (Student's *t*-test).

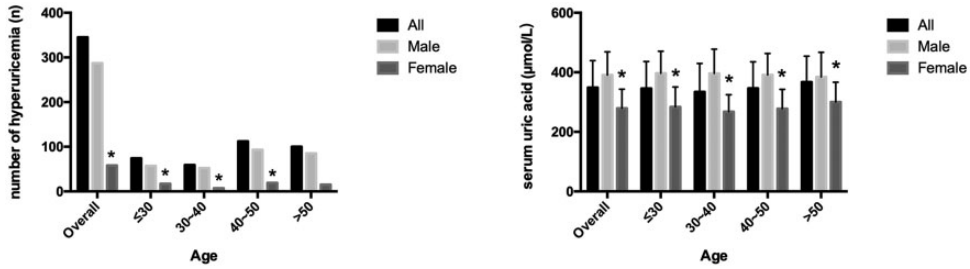


Figure 1. Hyperuricaemia rates (left) and serum uric acid levels (right) in 1393 individuals of Bai ethnicity categorized into different age groups. Data presented as *n* prevalence or mean \pm SD. * $P < 0.001$ male versus female (χ^2 -test or Student's *t*-test).

Table 2. Univariable correlation analysis showing an association between nutritional status and hyperuricaemia in 1393 individuals of Bai ethnicity.

Variable	All participants		Male		Female	
	<i>r</i>	Statistical significance	<i>r</i>	Statistical significance	<i>r</i>	Statistical significance
TC	0.203	$P < 0.001$	0.103	$P = 0.002$	0.186	$P < 0.001$
TG	0.266	$P < 0.001$	0.163	$P < 0.001$	0.296	$P < 0.001$
HDL-c	-0.131	$P < 0.001$	-0.037	NS	-0.127	$P = 0.004$
LDL-c	0.290	$P < 0.001$	0.162	$P < 0.001$	0.270	$P < 0.001$
Fasting glucose	0.044	NS	0.003	NS	0.142	$P < 0.001$
TP	0.093	$P < 0.001$	-0.304	NS	0.212	$P < 0.001$
Albumin	-0.014	NS	0.007	NS	-0.063	NS

TC, total cholesterol; TG, triglycerides; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; TP, total protein; *r*, correlation coefficient. NS, no statistically significant correlation ($P > 0.05$).

Table 3. Multivariable logistic regression analysis of nutritional status and related risk factors for hyperuricaemia in 1393 individuals of Bai ethnicity.

Variable	β	Wald value	OR (95% CI)	Statistical significance
TC	0.343	48.915	1.409 (1.280, 1.552)	$P < 0.001$
LDL-c	1.126	50.560	3.082 (2.260, 4.204)	$P < 0.001$

TC, total cholesterol; LDL-c, low-density lipoprotein cholesterol; β , regression coefficient; OR, odds ratio; CI, confidence interval.

concentrations were 173.57 ± 13.24 g/l and 145.97 ± 13.64 g/l. Out of 717 participants with polycythaemia, 241 (33.6%) also had hyperuricaemia, and of 676 participants without polycythaemia, 104 (15.4%) had

hyperuricaemia ($\chi^2 = 62.04$, $P < 0.001$), indicating that hyperuricaemia was significantly more prevalent in individuals with polycythaemia versus those without. Furthermore, participants with polycythaemia had

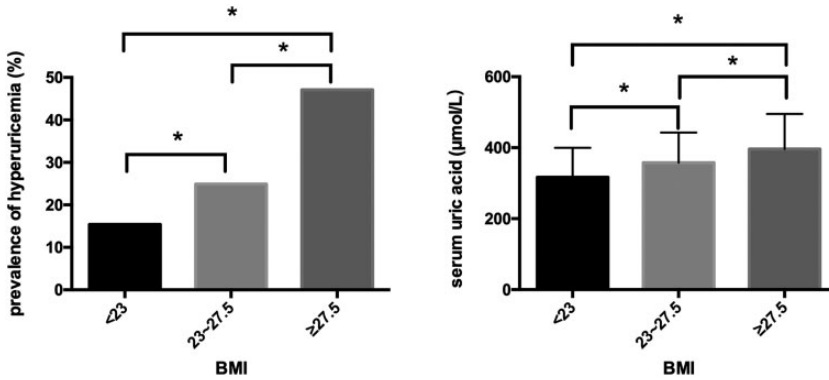


Figure 2. Hyperuricaemia prevalence rates (left) and serum uric acid levels (right) in 1393 individuals of Bai ethnicity categorized into different body mass index (BMI) groups. Data presented as % prevalence or mean \pm SD. * $P < 0.001$ (χ^2 -test or Student's t -test).

Table 4. Multivariable linear regression analysis of the associations between polycythaemia-related characteristics and serum uric acid levels in 1393 individuals of Bai ethnicity.

Variable	All			Male			Female		
	β value	t	Statistical significance	β value	t	Statistical significance	β value	t	Statistical significance
RBC	0.122	3.296	$P < 0.001$	0.039	0.851	NS	0.197	3.500	$P < 0.001$
Hb	0.432	6.656	$P < 0.001$	0.094	1.329	NS	0.229	2.656	$P = 0.008$
Hct	-0.041	-0.576	NS	-0.061	-0.806	NS	-0.157	-1.587	NS

RBC, red blood cell; Hb, haemoglobin; Hct, haematocrit. NS, no statistically significant correlation ($P > 0.05$).

significantly higher SUA levels versus those without (386.33 ± 77.21 versus 308.51 ± 7.03 , $P < 0.001$). Multivariate linear regression revealed that SUA levels were positively correlated with RBC and Hb in the all-participants group and in women, but not in men (Table 4). Logistic analysis revealed that polycythaemia and haemoglobin levels were risk factors for hyperuricaemia (Table 5).

Discussion

The current study investigated the prevalence of hyperuricaemia, and associated risk factors, in Bai individuals residing in

Yunnan Province, and obtained epidemiological data that may help improve the health status of this minority community. The prevalence of hyperuricaemia was 24.8%, and was markedly higher in males than females (33.2% versus 11.0%). SUA levels also varied by age, BMI, and nutritional status. Furthermore, a correlation was established between polycythaemia and hyperuricaemia: participants with polycythaemia had significantly higher SUA levels (386.33 ± 77.21 versus 308.51 ± 7.03) and hyperuricaemia prevalence compared with individuals without polycythaemia (33.6% versus 15.4%).

Table 5. Logistic regression analysis of risk factors associated with hyperuricaemia in 1393 individuals of Bai ethnicity.

Variable	β	Wald value	OR (95%CI)	Statistical significance
Polycythemia	0.466	4.579	1.594 (1.040, 2.442)	$P = 0.032$
Hb	0.019	9.982	1.019 (1.007, 1.031)	$P = 0.002$

Hb, haemoglobin; β , regression coefficient.

Hyperuricaemia prevalence is known to vary by region in China. The present study reported a higher prevalence rate of hyperuricaemia in Bai individuals (24.8% overall; 33.2% and 11.0% in men and women, respectively) compared with 8.4–13.3% reported for the general Chinese population.^{4,12}

Interestingly, elevated hyperuricaemia prevalence has been observed in the western region compared with the eastern region of China. For instance, the hyperuricaemia rate in employees residing on the Qinghai-Tibet Plateau is reported to be 28.1%,¹³ while a 37.2% rate (41% in men and 34.4% in women) was found in those inhabiting the Ganzi Tibetan Autonomous Prefecture.¹⁴ A cross-sectional study reported a hyperuricaemia prevalence of 21% in the Yi ethnic group,¹⁵ and a study focusing mainly on Tibetan farmers/herdsmen reported a hyperuricaemia prevalence of only 2.05%.¹⁶ These varying prevalence rates suggest that hyperuricaemia may be linked to dietary, geographical and ethnic factors.

As in previous reports,^{17,18} hyperuricaemia prevalence in the present study displayed a U-shaped association with age. Moreover, opposing trends in hyperuricaemia prevalence were observed in different sexes based on age, in that prevalence gradually declined with increasing age in men but was elevated in women aged 30–40 years. This phenomenon concurred with the findings of previous epidemiological studies.^{13,19,20}

In the present study population, the highest prevalence of hyperuricaemia in female participants occurred in those aged >50 years (22.4%). Other sex-specific differences in hyperuricaemia were also revealed, e.g. multivariate linear regression showed that SUA levels positively correlated with RBC and Hb in women but not in men, and these differences may be partly due to potential interactions among sex hormones.^{21,22} Our hypothesis conformed to the recently published CHIEF study, in which the authors found a greater association between hyperuricaemia and elevated blood pressure in women than in men, attributed mainly to the interaction of oestrogen.²³ Indeed, oestrogen is a natural uricosuric agent; hence, SUA is increased in post-menopausal females.²⁴ Sex differences in the associations between SUA and RBC or Hb levels may be explained by greater xanthine oxidase activity and production of reactive oxygen species caused by higher erythroblast turnover in women with higher SUA levels.

Levels of SUA are known to be associated with cardiovascular conditions, such as coronary artery disease,²⁵ and have a strong positive correlation with long-term variability in SBP and DBP in young males.²⁶ Dyslipidaemia is a well-recognized cardiovascular risk factor, and triglyceride and HDL-c levels have been demonstrated to independently predict hyperuricaemia.^{27,28} The inflammatory and oxidative reactions induced by SUA in adipocytes might underlie the complex interactions. Therefore, the

association between hyperuricaemia and dyslipidaemia was examined in the Bai ethnic group in the present study. Levels of triglyceride (OR 1.409, 95% CI 1.280, 1.552) and LDL-c (OR 3.082, 95% CI 2.260, 4.204) were found to be risk factors for hyperuricaemia, suggesting that local clinicians should consider both SUA and lipids as risk factors for cardiovascular diseases in Bai ethnic individuals.

Obesity also has an association with hyperuricaemia. For example, SUA was found to be positively correlated with obesity in 260 adults stratified into four quartiles based on SUA concentrations (Q1, <232 $\mu\text{mol/l}$; Q2, 232–291 $\mu\text{mol/l}$; Q3, 292–345 $\mu\text{mol/l}$; and Q4, >345 $\mu\text{mol/l}$), who showed markedly increased obesity prevalence rates of 17.4%, 22.2%, 28.6% and 31.8%, from Q1–4, respectively.²⁹ BMI, as a marker of the degree of obesity, partially mediates the association between SUA and diabetes risk.³⁰ In the present study, the overweight and obesity groups displayed increased hyperuricaemia prevalence rates and also significantly elevated SUA levels, indicating that appropriate weight management might help control SUA levels in the Bai ethnic population.

The mechanism underlying hyperuricaemia in the present study population in Jianchuan County may be multifactorial. In addition to common risk factors, prolonged exposure to high altitude might play an equally major role in disease occurrence. High-altitude living normally promotes polycythaemia, which is a beneficial response to high-altitude hypoxia.³¹ But polycythaemia itself is also recognized as a cardiovascular risk factor, as it may cause bleeding and thromboembolic events, and increase the risk of hypertension, particularly by decreasing nocturnal dipping.³² Although Jianchuan County does not unequivocally fulfil the criteria of high altitude (>2400 m above sea level),³³ more than half of the participants in the present study

displayed polycythaemia. As shown above, hyperuricaemia prevalence and SUA levels were significantly higher in subjects with polycythaemia than in those without. A possible explanation may be an increase in the synthesis of nucleic acids due to an erythropoietic response to chronic hypoxia. Moreover, individuals residing at high altitudes have reduced urinary fractional excretion of UA, despite increased UA production secondary to tissue ischaemia caused by hypoxaemia.³¹

The results of this study may be limited by several factors. First, the study was not prospective; hence, causal relationships could not be obtained. Secondly, personal dietary data were not included. Thirdly, the urinary fractional excretion of UA was not analysed due to measurement limitations of the laboratory. Thus, the current study only investigated risk factors for hyperuricaemia in the Bai ethnic group, and multicentre and prospective clinical studies are required to validate these findings.

In conclusion, the high prevalence of hyperuricaemia in individuals of Bai ethnicity residing in Yunnan Province (China) may be related to specific geographical and ethnic factors besides traditional risk factors, such as age, sex and BMI. The results of the current study may help design further studies and improve health-care strategies in this population. However, multicentre investigations are essential to comprehensively understand epidemiological mechanisms.

Acknowledgments

We thank the medical staff at the People's Hospital of Jianchuan County for support in this study.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This research was sponsored by Shanghai Sailing Program (20YF1428400), Shanghai Health Commission Scientific Research Project (20204Y0126), Shanghai Municipal Key Clinical Specialty (shslczdzk02502), and Zhongguancun Nephrology & Blood Purification Innovation Alliance Youth Research Fund (NBPIA20QC0302).

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