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ORIGINAL ARTICLE

Dissecting the risk factors for hyperuricemia in vegetarians in Taiwan

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Abstract

Background: Vegetarian diets have been shown to lower the risks of hyperuricemia and gout. Little is known about the risk factors of hyperuricemia in vegetarians.

Methods: This community-based retrospective case–control study was conducted to establish prediction models for hyperuricemia. From September 5, 2005, to December 31, 2016, 7331 adult vegetarians were recruited at Taipei Tzu Chi Hospital. Hyperuricemia was defined as a serum uric acid concentration greater than 7 mg/dL.

Results: There were 593 (8.1%) vegetarians with hyperuricemia and 6738 (91.9%) without hyperuricemia. We stepwise built up three models for predicting hyperuricemia in vegetarians. The full model (model 3) has the highest area under the receiver operating characteristic curve (AUROC, 85.52%). Additionally, the AUROC of model 3 is 77.97% and 84.85% in vegetarians with or without prior gout history, respectively. Moreover, male gender, hyperlipidemia, body mass index, and serum albumin are independent risk factors for hyperuricemia in vegetarians. In contrast, estimated glomerular filtration rate and proteinuria are independently associated with lower risks of hyperuricemia in vegetarians.

Conclusion: Our study revealed that risk factors for hyperuricemia, which includes clinical characteristics, account for more than 85% of discriminatory performance in Taiwanese vegetarians. This model may be helpful for monitoring and preventing hyperuricemia in the population.

Keywords: Hyperuricemia; Risk factor; Vegetarian

1. INTRODUCTION

Uric acid is the final oxidation product of purine metabolism in human beings. High uric acid concentration results from increased production, decreased excretion of uric acid, or a combination of both processes. The prevalence of hyperuricemia was above 21% based on the US National Health and Nutrition Examination Survey 2007-2008 study.[1] According to the statistics in 1993-1996, Taiwan was notably affected by a relatively high rate of hyperuricemia. There is 43.7% of hyperuricemia in men and 27.4% in women in Taiwan.[2]

At present, hyperuricemia is regarded as a serious public health problem. Hyperuricemia can result in gout[3] and is related to cardiovascular disease,[4,5] chronic kidney disease,[6] and cancer.[7–9] Specific dietary components are thought to affect concentrations of uric acid. Mainly, vegetarian diets may target multiple pathways in uric acid pathogenesis. Vegetarians consume more vegetables, whole grains, and nuts while away from purine-rich meat and seafood.[10,11] Compared with omnivores, vegetarians are considered to have a lower concentration of uric acid. However, there are some vegetarians who are still in the status of hyperuricemia. The reason is that there is a pile of other factors, such as body mass index (BMI) and age, linked to uric acid pathogenesis, while the causal nature of these relationships needs to be clarified.[8,12]

The independent risk factors for the incidence of hyperuricemia have been investigated a lot by former studies.[13–17] However, the previous research established an available prediction model of hyperuricemia,[18] but not for people consuming vegetarian diets. Therefore, we created predictive models of hyperuricemia for vegetarians using a large population-based cohort in Taiwan. This study aims to help vegetarians discover other risk factors and avoid more adverse effects associated with hyperuricemia.

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2. METHODS

2.1. Design and study participants

Fig. 1 illustrates the enrollment for the study. This retrospective cross-sectional study was conducted to create a model to predict hyperuricemia based on demographics, comorbidities, and commonly available biochemistry tests in vegetarians. We enrolled individuals aged above 40 years and underwent health exams and food questionnaires at the Health Examination Center of Taipei Tzu Chi Hospital (New Taipei City, Taiwan) from September 5, 2005, to December 31, 2016. Omnivores, subjects aged <40, and those with incomplete demographic information or biochemical data were excluded (Fig. 1). The study was conducted in accordance with the Declaration of Helsinki and was approved by the institutional review board at the Taipei Tzu Chi Hospital (approval number: 07-X-104). Informed consent was waived because of the retrospective study design.

2.2. Clinical assessment

A validated food questionnaire was used for evaluating dietary patterns. Diet categories were divided into vegan, lacto-ovo vegetarian, and omnivore. Lacto-ovo vegetarians were defined as consuming eggs, dairy products, or both but without other animal products. Vegans were defined as consuming exclusively vegetables and fruits. Omnivores were defined as consuming both plant-based and animal-based foods. The structured questionnaire containing questions about age, gender, medical history, and functional health patterns was completed by a well-trained nurse at the entry of the study. Height and weight were measured using an automatic electronic meter (SECA GM-1000, Seoul, Korea) for calculating the BMI (kg/m^2). An automatic blood pressure machine (Welch Allyn 53000, New York, NY, USA) was used to measure blood pressure. Venous blood was drawn after at least 8 hours of fasting. Measurements included serum creatinine, albumin, glycated hemoglobin (HbA1c), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and uric acid (Dimension RXL Max integrated chemistry system; Siemens, Erlangen, Germany). The estimated glomerular filtration rate (eGFR) was calculated by using the creatinine-based Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[19] Urine protein was tested using a single dipstick analysis with an automated urine analyzer (Arkray 4030, Tokyo, Japan). These results were reported as a 6-grade scale: absent (<10 mg/dL), trace (+/–) (10-20 mg/dL), 1+ (30 mg/dL), 2+ (100 mg/dL), 3+ (300 mg/dL), or 4+ (>1000 mg/dL). Proteinuria was defined as trace, 1+, or above. CKD was defined as either the presence of proteinuria or an eGFR of ≤60 mL/min per 1.73 m^2.[20]

2.3. Outcome measures

Hyperuricemia was defined as the concentration of serum uric acid level greater than 7.0 mg/dL based on the Taiwan Guideline for the Management of Gout and Hyperuricemia.[21]

2.4. Statistical analyses

Data are expressed as number (percentage) or mean (SD). Student's *t*-test and Chi-square test compared the means and proportions between the two groups. Receiver operating characteristic (ROC) curves were used to illustrate the diagnostic performance of three different prediction models. The models were built up stepwise based on traditional risk factors of hyperuricemia or gout and other clinical characteristics of the participants.[19] Logistical regression was used to determine each variable's odds ratio (OR) with hyperuricemia in all models. The covariates in multivariable logistical regressions were age and sex (model 1); age, sex, diabetes, hypertension, hyperlipidemia, and proteinuria (model 2); age, sex, diabetes, hypertension, hyperlipidemia, and proteinuria, eGFR, systolic blood pressure, HbA1c, HDL-C, LDL-C, BMI, serum albumin, alcohol drinking, and dietary habits (model 3, fully adjusted model). A two-tailed p value of less than 0.05 was considered statistically significant. All statistical analyses were performed using SAS software (version 9.4; SAS Institute Inc., Cary, NC) and STATA (version 15.1; Stata Corp, College Station, TX).

3. RESULTS

3.1. Patient characteristics

A total of 7331 vegetarians entered the final analyses. Table 1 shows the demographic and clinical information in patients with (n = 593) or without (n = 6738) hyperuricemia. Compared with patients without hyperuricemia, those with hyperuricemia were older (62.2 ± 10.3 vs 60.9 ± 9.4 years old, p = 0.001); predominantly male (74.9% vs 29.2%, p < 0.001); more had alcohol drinking (8.9% vs 5.6%, p = 0.001), hypertension (33.7% vs 17.6%,

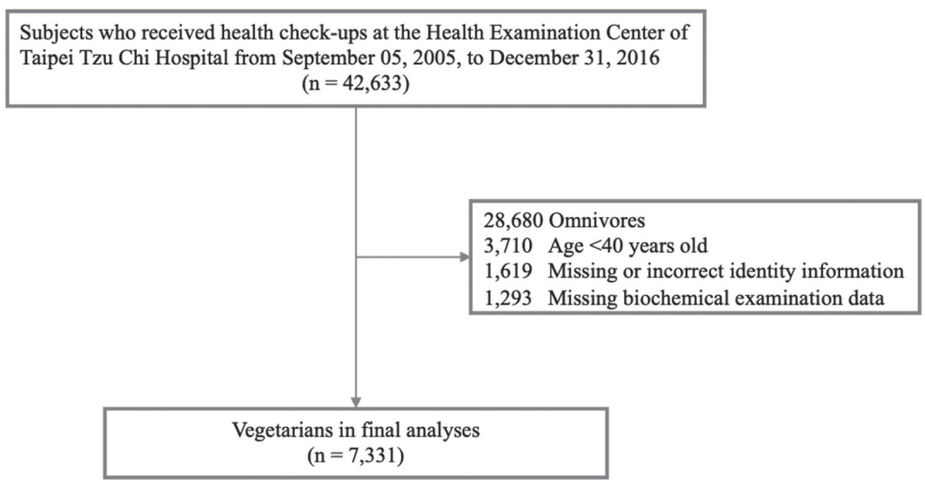

Fig. 1 Flowchart of patient selection. The database included 42 633 individuals who received physical checkups at the Health Examination Center of Taipei Tzu Chi Hospital. After excluding subjects younger than 40 y old (n = 3710), those with incomplete identification information (n = 1619) or missing biochemical data (n = 1293), and omnivores (n = 28,680). Finally, there were 7331 vegetarians entered the final analyses.

Table 1

The demographics, comorbidities, and biochemical examinations in vegetarians with or without hyperuricemia

Characteristics	With hyperuricemia (n = 593)	Without hyperuricemia (n = 6738)	*p*
Age group, y, n (%)			
40-49	69 (11.6)	797 (11.8)	0.89[a]
50-69	181 (30.5)	2245 (33.3)	0.17[a]
60-69	209 (35.2)	2546 (37.8)	0.22[a]
≥70	134 (22.6)	1150 (17.1)	0.001[a]
Age, y, mean (SD)	62.2 (10.3)	60.9 (9.4)	0.001[b]
Gender, n (%)			
Male	444 (74.9)	1965 (29.2)	<0.001[a]
Female	149 (25.1)	4773 (70.8)	<0.001[a]
Current smoking, n (%)	7 (1.2)	38 (0.6)	0.07[a]
Alcohol drinking, n (%)	53 (8.9)	374 (5.6)	0.001[a]
BMI, kg/m^{2,} mean (SD)	25.3 (3.8)	22.9 (3.2)	<0.001[b]
>27, n (%)	151 (25.5)	707 (10.5)	<0.001[a]
Hypertension, n (%)	200 (33.7)	1187 (17.6)	<0.001[a]
SBP, mmHg, mean (SD)	126 (15)	119 (15)	<0.001[b]
Diabetes, n (%)	56 (9.4)	393 (5.8)	<0.001[a]
HbA1c, %, mean (SD)	5.7 (0.8)	5.6 (0.8)	0.08[b]
AST, IU/L, mean (SD)	26.5 (13.9)	22.5 (20.0)	<0.001[b]
ALT, IU/L, mean (SD)	33.5 (23.3)	25.5 (20.1)	<0.001[b]
HDL-C, mg/dL, mean (SD)	42.4 (11.6)	51.4 (14.8)	<0.001[b]
LDL-C, mg/dL, mean (SD)	119.3 (30.8)	116.1 (30.4)	0.07[b]
Serum albumin, g/dL, mean (SD)	4.3 (0.4)	4.2 (0.3)	<0.001[b]
Gout history, n (%)	130 (21.9)	132 (2.0)	<0.001[a]
Proteinuria, n (%)	92 (15.5)	1054 (15.6)	0.93[a]
Serum creatinine, mg/dL, mean (SD)	1.1 (0.6)	0.8 (0.3)	<0.001[b]
eGFR[c], mL/min/1.73 m^2, mean (SD)	76 (17)	87 (13)	<0.001[b]
CKD, n (%)	160 (27.0)	1223 (18.2)	<0.001[a]
CKD stage, n (%)			
3	132 (22.3)	1177 (17.5)	<0.001[a]
4-5	12 (2.0)	18 (0.3)	<0.001[a]

ALT = alanine aminotransferase; AST = aspartate aminotransferase; BMI = body mass index; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; HbA1c = glycated hemoglobin; HDL-C = high-density lipoprotein cholesterol; IU = international unit; LDL-C = low-density lipoprotein cholesterol; OR = odds ratio; SBP = systolic blood pressure.

[a]Chi-square test.

[b]Student's *t* test.

[c]Calculated by using the Chronic Kidney Disease Epidemiology Collaboration formula.

$p < 0.001$), diabetes mellitus (9.4% vs 5.8%, $p < 0.001$), CKD (27% vs 18.2%, $p < 0.001$) and history of gout (21.9% vs 2%, $p < 0.001$); and had higher BMI (25.3 ± 3.8 vs 22.9 ± 3.2, $p < 0.001$), higher aspartate aminotransferase (26.5 ± 13.9 vs 22.5 ± 20, $p < 0.001$), higher alanine aminotransferase (33.5 ± 23.3 vs 25.5 ± 20.1, $p < 0.001$), lower HDL-C (42.4 ± 11.6 vs 51.4 ± 14.8 mg/dL, $p < 0.001$), higher albumin (4.3 ± 0.4 vs 4.2 ± 0.3 mg/dL), higher creatinine (1.1 ± 0.6 vs 0.8 ± 0.3 mg/dL, $p < 0.001$), and lower CKD-EPI eGFR (76 ± 17 vs 87 ± 13 mL/min/1.73 m^2, $p < 0.001$) values.

3.2. ROC curves for prediction of hyperuricemia

Fig. 2 shows the ROC curves of three models for predicting hyperuricemia in vegetarians. Model 1 includes age and gender. The area under the ROC curve of model 1 is 75.72%. In addition, model 2 includes variables in model 1 plus diabetes mellitus, hypertension, hyperlipidemia, and proteinuria. The area under the ROC curve of model 2 is 81.01%. Moreover, model 3 includes variables in model 2 and eGFR, systolic blood pressure, glycated hemoglobin, HDL-C, LDL-C, BMI, albumin, alcohol drinking, and dietary habits (vegan vs lacto-ovo vegetarian diets). The area under the ROC curve of model 3 is 85.52%, the highest among the three models. Fig. 3A illustrates the ROC curves of different prediction models for hyperuricemia in vegetarians without gout history. The area under the ROC curves is 64.59%, 70.17%, and 77.97% for model 1, model 2, and model 3, respectively. With regard to vegetarians with gout history, the area under the ROC curves is 75.16%, 79.81%, and 84.85% for model 1, model 2, and model 3, respectively (Fig. 3B).

3.3. Multivariable logistic regression models

Table 2 shows the association of each variable with the presence of hyperuricemia in the three models in vegetarians. In model 1, age (adjusted OR: 1.01 per year, $p = 0.002$) and male gender (adjusted OR: 7.22, $p < 0.001$) are independent risk factors for hyperuricemia. After adding diabetes mellitus, hypertension, hyperlipidemia, and proteinuria into the model (model 2), age (adjusted OR: 1.02 per year, $p = 0.008$), male gender (adjusted OR: 15.8, $p < 0.001$), hypertension (adjusted OR: 1.84, $p < 0.001$), and hyperlipidemia (adjusted OR: 1.08, $p < 0.001$) are independent risk factors for hyperuricemia. In the fully adjusted model (model 3), male gender (adjusted OR: 8.29, $p < 0.001$), hyperlipidemia (adjusted OR: 1.04, $p = 0.024$), BMI (adjusted OR: 1.13 per kg/m^2, $p < 0.001$), and serum albumin (adjusted OR: 2.18 per g/dL, $p = 0.001$) are independent risk factors for hyperuricemia in vegetarians. In contrast, proteinuria (adjusted OR: 0.66, $p = 0.01$) and eGFR (adjusted OR: 0.95 per mL/min/1.73 m^2, $p < 0.001$) are associated with lower risks of hyperuricemia in vegetarians.

With regard to participants without gout history (Table 3), male gender (adjusted OR: 6.54, $p < 0.001$), hyperlipidemia (adjusted OR: 1.03, $p = 0.046$), BMI (adjusted OR: 1.12 per

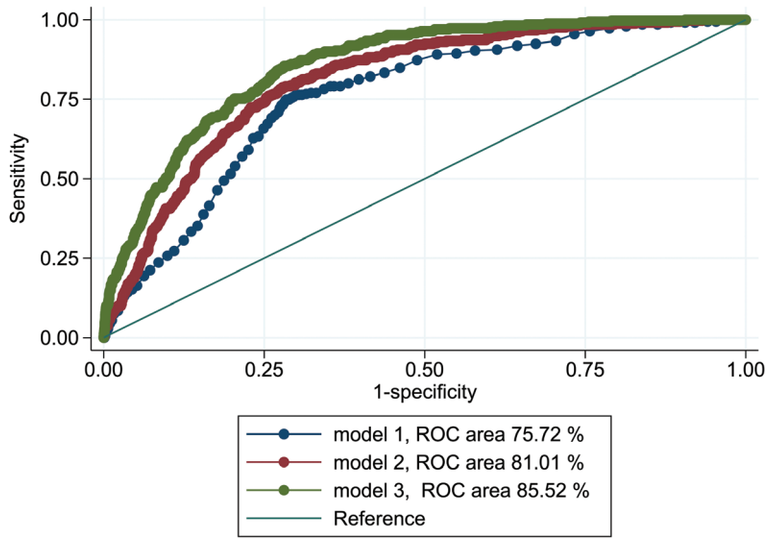

Fig. 2 The ROC curves of prediction models for hyperuricemia in vegetarians. Model 1: adjusted for age and gender. Model 2: adjusted for the variables in model 1 and diabetes, hypertension, hyperlipidemia, and proteinuria. Model 3: adjusted for the variables in model 2 and estimated glomerular filtration rate, systolic blood pressure, glycated hemoglobin, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, body mass index, serum albumin, alcohol drinking, and dietary patterns (lacto-ovo vegetarian vs vegan diet). ROC = receiver operating characteristic.

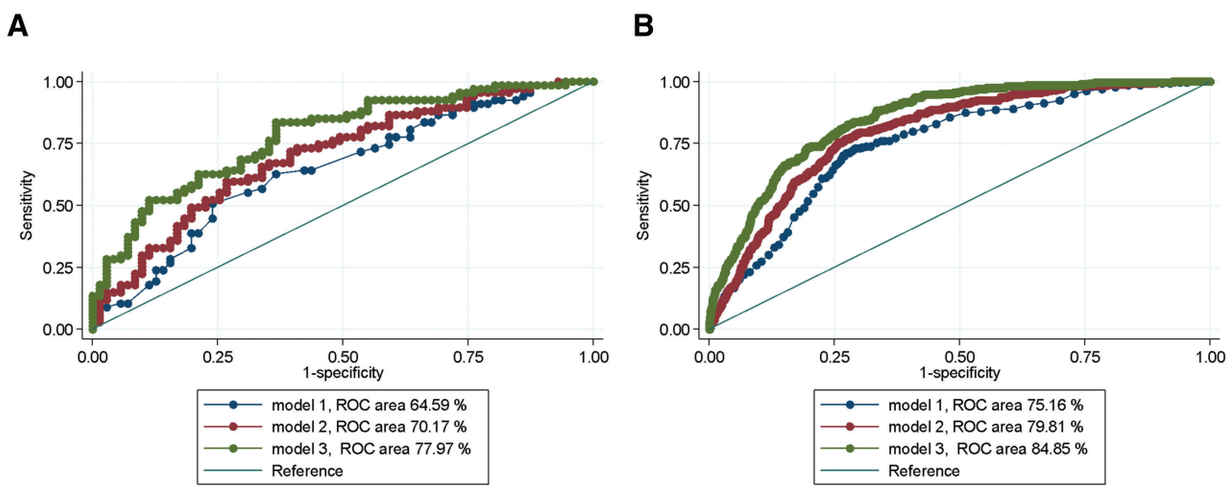

Fig. 3 The ROC curves of prediction models for hyperuricemia in vegetarians with (A) or without (B) gout history. Model 1: adjusted for age and gender. Model 2: adjusted for the variables in model 1 and diabetes, hypertension, hyperlipidemia, and proteinuria. Model 3: adjusted for the variables in model 2 and estimated glomerular filtration rate, systolic blood pressure, glycated hemoglobin, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, body mass index, serum albumin, alcohol drinking, and dietary patterns (lacto-ovo vegetarian vs vegan diet). ROC = receiver operating characteristic.

kg/m^2, p = 0.001), and serum albumin (adjusted OR: 2.73 per g/dL, p < 0.001) are independent risk factors for hyperuricemia in vegetarians. However, eGFR (adjusted OR: 0.95 per mL/min/1.73 m^2, p < 0.001) and HDL-C (adjusted OR: 0.98 per mg/dL, p = 0.001) are independently associated with lower risks for hyperuricemia in vegetarian (model 3). Among those with gout history, male gender (adjusted OR: 9.47, p = 0.012) and HDL-C (adjusted OR: 1.06 per mg/dL, p = 0.012) are independent risk factors for hyperuricemia in vegetarians. In contrast, age (adjusted OR: 0.89 per year, p < 0.001) and eGFR (adjusted OR: 0.94 per mL/min/1.73 m^2, p = 0.001) are independently linked to lower risks for hyperuricemia in vegetarians (Table 3).

4. DISCUSSION

We found that male gender, hyperlipidemia, BMI, and serum albumin are independent risk factors for hyperuricemia in vegetarians. In contrast, proteinuria and eGFR are associated with lower risks of hyperuricemia in vegetarians. Then, we created the first predictive model of hyperuricemia for vegetarians in Taiwan. The area under the fully adjusted model's (model 3) ROC curve is 85.52%. We also created different prediction models for vegetarians with or without prior gout, in which the area under the ROC curves is 77.97% and 84.85%, respectively. These models may help to predict and avoid hyperuricemia for vegetarians.

Table 2

Multiple logistic regression models for hyperuricemia in vegetarians

	Model 1[a]		Model 2[b]		Model 3[c]	
	Adjusted OR (95% CI)	*p*	Adjusted OR (95% CI)	*p*	Adjusted OR (95% CI)	*p*
Age, per year	1.01 (1.00-1.02)	0.002	1.02 (1.00-1.03)	0.008	0.98 (0.97-1.00)	0.07
Male vs female	7.22 (5.95-8.76)	<0.001	15.8 (11.4-22.1)	<0.001	8.29 (5.32-12.9)	<0.001
Diabetes			0.98 (0.65-1.48)	0.92	0.92 (0.54-1.58)	0.76
Hypertension			1.84 (1.40-2.40)	<0.001	1.28 (0.95-1.73)	0.11
Hyperlipidemia			1.08 (1.06-1.10)	<0.001	1.04 (1.00-1.07)	0.024
Proteinuria			0.80 (0.60-1.08)	0.14	0.66 (0.48-0.90)	0.01
eGFR[d], per mL/min/1.73 m^2					0.95 (0.94-0.96)	<0.001
HbA1c, %					0.87 (0.72-1.00)	0.13
SBP, per 10 mmHg					1.00 (0.91-1.09)	0.93
HDL-C, per mg/dL					0.99 (0.98-1.00)	0.06
LDL-C, per mg/dL					1.04 (0.99-1.08)	0.1
BMI, per kg/m^2					1.13 (1.06-1.20)	<0.001
Serum albumin, per g/dL					2.18 (1.37-3.46)	0.001
Alcohol drinking					0.80 (0.50-1.28)	0.36
Lacto-ovo vegetarian vs vegan diet					1.17 (0.83-1.66)	0.36

BMI = body mass index; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; HbA1c = glycated hemoglobin; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; OR = odds ratio; SBP = systolic blood pressure.

[a]Adjusted for age and gender.

[b]Adjusted for the variables in model 1 and diabetes, hypertension, hyperlipidemia, and proteinuria.

[c]Adjusted for the variables in model 2 and eGFR, SBP, HbA1c, HDL-C, LDL-C, BMI, serum albumin, alcohol drinking, and lacto-ovo vegetarian vs vegan diet.

[d]Calculated by using the Chronic Kidney Disease Epidemiology Collaboration formula.

According to the Nutrition and Health Survey in Taiwan 2005-2008, the prevalence of hyperuricemia in the groups aged 19-45, 45-64, and ≥65 years was 22.1%, 18.8%, and 25.8% in men and 4.3%, 9.1%, and 33.6% in women, respectively.[22] Our data show that the prevalence of hyperuricemia in vegetarians or lacto-ovo vegetarians is 8.08%. This is similar to a previous study, which shows that 9.3% of vegetarians had hyperuricemia in Taiwan.[23] There is a lower prevalence of hyperuricemia in vegetarians than in omnivores. The reason may be that poultry, meat, and fish are all purine-rich food, and purine is well known as the source of uric acid. This is not surprising for vegetarians had a lower risk of hyperuricemia[24] and even had a lower risk for gout.[25]

There is a higher incidence rate of hyperuricemia for males than for females in the omnivore diet.[13,14] This is similar to our study (74.9% vs 25.1%). Age, male gender, alcohol drinking, BMI, systolic blood pressure, diabetes, high low-density lipoprotein, low-density lipoprotein, prior gout, and serum creatinine are traditional risk factors for hyperuricemia in omnivore diet.[13–17] Our study reveals risk factors such as male gender (adjusted OR: 8.29, $p < 0.001$), hyperlipidemia (adjusted OR: 1.04, $p = 0.024$), BMI (adjusted OR: 1.13 per kg/m^2, $p < 0.001$), and serum albumin (adjusted OR: 2.18 per g/dL, $p = 0.001$) are independent risk factors for hyperuricemia in vegetarians. Different from hyperuricemia in an omnivore diet, serum albumin is the particular risk factor for hyperuricemia in our study. Vegetarians with higher serum albumin may intake more soy food, which is the primary protein source in vegetarians. There is a high purine content in soy food. Soy food is considered the risk for gout or hyperuricemia in 48% of health professionals in Asia.[26] However, in Chiu et al's[23] study, high soy intake among Taiwanese vegetarians shows no increased risk of hyperuricemia. On the other hand, serum albumin is a negative acute-phase protein that decreases during chronic inflammation. Hyperuricemia has been reported to induce low-grade inflammation. In this theory, higher serum albumin may be related to a lower risk of hyperuricemia.[27] Thus, further investigation still needs to explore the relationship between serum albumin and hyperuricemia in vegetarians.

On the contrary, proteinuria is a parameter that correlates to CKD. Thus, proteinuria is seen as an increased risk of hyperuricemia in an omnivore diet.[28] Our findings show that higher eGFR has a lower risk for hyperuricemia in a vegetarian diet (adjusted OR: 0.95 per mL/min/1.73 m^2, $p < 0.001$). However, proteinuria is related to a low risk of hyperuricemia (adjusted OR: 0.66, $p = 0.01$). This controversy may be related to our urine analysis is checked by urine dipstick, which is easily underestimated proteinuria if urine is diluted.[29] Besides, diabetes is well known as a traditional risk for hyperuricemia in the omnivore diet.[13,15] In Chiu et al's[23] study, both hyperglycemia and diabetes are at high risk of hyperuricemia in vegetarians. However, HbA1c is not associated with hyperuricemia in vegetarians in the current study. Further studies are needed to clarify this issue.

Cao et al[18] created gender-specific prediction models for hyperuricemia whose predictors of hyperuricemia were age, BMI, systolic blood pressure, serum uric acid for males, and BMI, systolic blood pressure, serum uric acid, triglycerides for females. The models' *c* statistics were 0.783 (95% CI, 0.779-0.786) for males and 0.784 (95% CI, 0.778-0.789) for females.[18] Our findings do not contradict Cao et al's[18] study; even our ROC curve of model 3 is 85.52%, which is more sensitive. We also make different prediction models for vegetarians with or without prior gout. Our study's area under the ROC curve without gout history is 84.85%, stronger than that with gout history (77.97%).

Besides, it is well known as some hyperuricemia areas related to genetic predisposition. Recent studies showed that different changes in urate transporters are associated with hyperuricemia. The apical URAT1 and the basolateral GLUT9 are the main reabsorptive urate transporters. GLUT9 are the main reabsorptive urate transporters. Loss-of-function mutations of the SLC22A12 cause type 1 renal hypouricemia, and mutation of the SLC2A9 gene cause type 2 renal hypouricemia.[30] The ATP-binding cassette transporter (ABCG2) is an important urate transporter. Dysfunction of ABCG2 reduces cellular urate efflux and causes hyperuricemia and early-onset gout.[31]

On the other hand, some studies revealed that high fructose intake could lead to hyperuricemia.[32,33] In the liver, fructose

Table 3

Multiple logistic regression models for hyperuricemia in vegetarians by gout history

	Model 1[a]		Model 2[b]		Model 3[c]	
	Adjusted OR (95% CI)	*p*	Adjusted OR (95% CI)	*p*	Adjusted OR (95% CI)	*p*
Without gout history						
Age, per year	1.02 (1.01-1.03)	<0.001	1.03 (1.01-1.04)	<0.001	1.00 (0.98-1.02)	0.92
Male vs female	6.22 (5.05-7.66)	<0.001	13.7 (9.56-19.5)	<0.001	6.54 (4.05-10.6)	<0.001
Diabetes			1.03 (0.65-1.61)	0.91	0.97 (0.54-1.75)	0.92
Hypertension			1.59 (1.18-2.14)	0.002	1.12 (0.80-1.56)	0.52
Hyperlipidemia			1.08 (1.06-1.10)	<0.001	1.03 (1.00-1.07)	0.046
Proteinuria			0.90 (0.66-1.23)	0.52	0.74 (0.53-1.04)	0.08
CKD-Epi eGFR, per mL/min/1.73 m^2					0.95 (0.94-0.96)	<0.001
HbA1c, %					0.81 (0.66-1.01)	0.06
Systolic blood pressure, per 10 mmHg					0.98 (0.89-1.08)	0.65
High-density lipoprotein, per mg/dL					0.98 (0.97-0.99)	0.001
Low-density lipoprotein, per mg/dL					1.03 (0.99-1.08)	0.15
BMI, per kg/m^2					1.12 (1.05-1.19)	0.001
Serum albumin, per g/dL					2.73 (1.64-4.53)	<0.001
Alcohol drinking					0.80 (0.47-1.36)	0.41
Lacto-ovo vegetarian vs vegetarian diet					1.17 (0.81-1.70)	0.41
With gout history						
Age, per years old	0.98 (0.95-1.00)	0.06	0.96 (0.92-1.00)	0.042	0.89 (0.83-0.94)	<0.001
Male vs female	2.21 (1.12-4.36)	0.022	4.02 (1.16-13.9)	0.028	9.47 (1.65-54.3)	0.012
Diabetes			0.63 (0.19-2.11)	0.46	1.56 (0.29-8.34)	0.61
Hypertension			2.09 (0.99-4.43)	0.053	1.29 (0.51-3.28)	0.59
Hyperlipidemia			1.03 (0.98-1.09)	0.24	1.04 (0.94-1.15)	0.44
Proteinuria			0.59 (0.22-1.57)	0.29	0.59 (0.20-1.79)	0.35
eGFR[d], per mL/min/1.73 m^2					0.94 (0.91-0.97)	0.001
HbA1c, %					0.74 (0.48-1.13)	0.16
Systolic blood pressure, per 10 mmHg					1.11 (0.81-1.53)	0.52
HDL-C, per mg/dL					1.06 (1.01-1.11)	0.012
LDL-C, per mg/dL					1.06 (0.89-1.26)	0.52
BMI, kg/m^2					1.15 (0.97-1.37)	0.11
Serum albumin, per g/dL					0.61 (0.14-2.75)	0.52
Alcohol drinking					0.97 (0.24-3.99)	0.99
Lacto-ovo vegetarian vs vegan diet					1.13 (0.35-3.67)	0.84

BMI = body mass index; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; HbA1c = glycated hemoglobin; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; OR = odds ratio.

[a]Adjusted for age and gender.

[b]Adjusted for the variables in model 1 and diabetes, hypertension, hyperlipidemia, and proteinuria.

[c]Adjusted for the variables in model 2 and eGFR, SBP, HbA1c, HDL-C, LDL-C, BMI, serum albumin, alcohol drinking, and lacto-ovo vegetarian vs vegan diet.

[d]Calculated by using the Chronic Kidney Disease Epidemiology Collaboration formula.

metabolism reduces ATP and intracellular phosphate during metabolism, causing the conversion of AMP to IMP and stimulating the production of uric acid. In the kidney, fructose metabolism is associated with reducing urinary uric acid excretion and causing hyperuricemia.[34] It is possible that although vegetarians intake less purine, they may intake more fructose, leading to hyperuricemia.

In our study, we have created the first predictive model of hyperuricemia for vegetarians according to the population-based cohort in Taiwan. However, there are still a few limitations to this study. First, this is a self-reported cohort study. It may be an error when the patient recalls his history. Second, this is a case–control study. We cannot avoid weak associations between exposure and response. Third, the study population was from a single institute; most patients were Buddhist. The vegetarian diet content may be quite different between Buddhists and non-Buddhists. Fourth, most of the patients are from the Han Taiwanese population. This model may not be suitable for other ethics or nations. Finally, we do not collect medication data, such as diuretics. Diuretics use is considered as the risk of hyperuricemia. Thus, there is still a need for further prospective studies to confirm our model.

In conclusion, the risk factors of hyperuricemia for vegetarians in Taiwan, including large community-based patients, show more than 86% discriminatory performance. This model may be helpful for monitoring and preventing hyperuricemia in vegetarians.

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