

Allele C of rs6068816 in the *CYP24A1* Gene is Associated with Increased Risk of Hyperuricemia in the Chinese Population: A Case-Control Study

Jiahong Shangguan¹, Wenjing Zhang¹, Xiaodan Zhu¹, Yingying Zheng², Rui Xue³, Lili Xiao¹, Gangqiong Liu^{1,*}

¹Department of Cardiology, The First Affiliated Hospital of Zhengzhou University, 450052 Zhengzhou, Henan, China

²Department of Cardiology, Xinjiang Medical University Affiliated First Hospital, 830000 Urumqi, Xinjiang, China

³Medical Research Center, The First Affiliated Hospital of Zhengzhou University, 450052 Zhengzhou, Henan, China

*Correspondence: doctorliu61352@163.com (Gangqiong Liu)

Published: 20 November 2024

Background: Vitamin D (1,25-(OH)₂D) has been reported to be associated with hyperuricemia in many epidemiologic reports. *CYP24A1* is a rate-limiting enzyme involved in vitamin D metabolism. The aim of this study was to investigate the association between the rs6068816 polymorphism in the *CYP24A1* gene and hyperuricemia.

Methods: 130 patients with hyperuricemia from the First Affiliated Hospital of Zhengzhou University were included as the case group. 130 subjects without hyperuricemia were selected as the control group to establish a 1:1 matching case-control study. Logistic regression was used to investigate the association between rs6068816 and hyperuricemia. Additionally, multifactor dimensionality reduction analysis was used to further evaluate the interaction of rs6068816 and body mass index.

Results: The results indicated that patients with hyperuricemia had a higher frequency of genotype CT (Odds Ratio (OR): 2.494, 95% Confidence Interval (CI): 1.140–5.454, $p = 0.020$) and CC (OR: 3.375, 95% CI: 1.500–7.593, $p = 0.003$) than TT. The mean serum uric acid level for genotype CC was significantly higher than that of genotype TT ($p = 0.001$). People with genotype CC had a higher risk of developing hyperuricemia than genotype TT (OR: 5.061, 95% CI: 1.582–16.195, $p = 0.006$). Furthermore, rs6068816 had a significant multiplicative interaction with body mass index. Compared with genotype TT body mass index, CC body mass index displayed a higher risk of hyperuricemia (OR: 11.308, 95% CI: 1.420–90.049, $p = 0.022$). This interaction was further verified by the multifactor dimensionality reduction model with a cross-validation consistency of 10/10 and testing balanced accuracy of 0.696 ($p = 0.044$).

Conclusions: Genotype CC of rs6068816 in the *CYP24A1* gene is associated with a higher risk of hyperuricemia, especially for overweight people.

Keywords: *CYP24A1*; hyperuricemia; rs6068816; single nucleotide polymorphism (SNP); vitamin D

Introduction

Serum uric acid (SUA) is the final product of purine metabolism in humans. Abnormalities in uric acid metabolism, such as overproduction and reduced excretion from the kidneys, can lead to hyperuricemia [1]. Recent studies on the epidemiology of hyperuricemia have revealed increasing prevalence. For example, a large cohort study involving 38,885 people in Henan rural areas revealed that the hyperuricemia crude prevalence was 10.24% and the age-standardized prevalence was 12.60%. Moreover, the rate of increase of hyperuricemia in urban areas is higher than that of rural areas [2]. Hyperuricemia has been recognized as a possible factor in the onset of various chronic ailments, including, but not limited to, type 2 diabetes, obesity, metabolic syndrome, cardiovascular disease, stroke, hypertension, and renal dysfunction [3–7]. There-

fore, there is an urgent need to assess the risk factors for hyperuricemia to establish rational and effective measures for its prevention and control.

A previous study reported that insufficient levels of vitamin D (1,25-(OH)₂D) were associated with an elevated likelihood of developing hyperuricemia [8]. Furthermore, hyperuricemia is commonly associated with obesity, and studies have demonstrated that reducing body weight can lead to a reduction in serum uric acid levels [9]. Inadequate levels of vitamin D could also potentially play a role in the onset of obesity [10]. *CYP24A1* plays a crucial role in the regulation of vitamin D levels by facilitating the conversion of the active metabolite of vitamin D into 24-hydroxylated products for elimination [11]. Variation in *CYP24A1* may be related to vitamin D deficiency, obesity, and hyperuricemia. Based on the evidence above, we hypothesized that functional gene single nucleotide polymor-

phisms (SNPs) in *CYP24A1* and their interaction with body mass index (BMI) might be associated with hyperuricemia risk.

In this study, the association between rs6068816 in *CYP24A1* gene and hyperuricemia was investigated by a 1:1 matching case-control study, including 130 hyperuricemia patients and 130 healthy controls. The results provide valuable information for genetic risk assessment of hyperuricemia.

Materials and Methods

Study Subjects

In this study, an analysis was conducted on a group of 130 patients with hyperuricemia who were admitted to the First Affiliated Hospital of Zhengzhou University (Ethics Approval Number: KY-2020-0047). They were recruited for this study and designated as the case group. 130 healthy people who had no history of cancer, nephropathy, diabetes, or any other metabolic diseases were selected as the control group by 1:1 case-control matching; subjects were matched according to gender, age (no more than 5 years older or younger), and exposure to tobacco and alcohol. Individuals who had serum uric acid levels higher than 7.0 mg/dL for males and 6.0 mg/dL for females were categorized as having hyperuricemia.

The research was conducted following the guidelines stated in the Declaration of Helsinki, and approved by the Life Science Ethics Committee of Zhengzhou University (Ethics Approval Number: KY-2020-0047). And written informed consent was obtained from all participants.

Selection and Genotyping of *CYP24A1* SNPs

According to the literature, SNPs including rs4809957, rs6068816, rs6013897, and rs2248359 in the *CYP24A1* gene were reported to be associated with bone mineral density, blood pressure, gestational diabetes mellitus, and cancer risk [12–15]. Subsequently, rs6068816 was selected for further investigation in this study based on a pilot study including 30 cases and 30 controls. The whole blood samples were subjected to deoxyribonucleic acid (DNA) extraction using AU18019-96 DNA extraction kits (DP1902, Biotek corporation, Beijing, China). Polymerase chain reaction (PCR) amplification was performed using a 25 μ L reaction mixture containing the final concentrations as follows: 10.25 μ L of ddH₂O, 12.5 μ L Taqman Master Mix (2 \times), 1.25 μ L TaqMan SNP genotyping reagent solution (20 \times), and 1 μ L genomic DNA sample dilution. PCR conditions were as follows: denaturing at 95 $^{\circ}$ C for 10 minutes, and then modified (92 $^{\circ}$ C for 15 seconds) and annealing/extensions (60 $^{\circ}$ C for 60 seconds); repeated for 40 cycles. Samples were then analyzed using the 7500-fast real-time fluorescence quantitative PCR instrument (Applied Biosystems, Foster City, CA, USA).

Collection of Demographic and Anthropometric Information

Professionally trained investigators conducted in-person interviews with the participants, utilizing standardized questionnaires to collect data on their demographic attributes (including age, gender, education level, marital status, and occupation) as well as lifestyle aspects such as tobacco usage and alcohol consumption. Anthropometric measurements primarily included height and weight, with BMI calculated as body weight (kg) divided by height squared (m²). As per the Guidelines for Chinese Residents, individuals with a BMI below 18.5 were classified as underweight, while those with a BMI ranging from 18.5 to 24.0 were considered normal weight. Overweight was defined as having a BMI between 24.0 and 28.0, whereas obesity refers to individuals whose BMI exceeded 28 [16].

Biochemical Measurements

All participants were instructed to fast for at least 8 hours, and their blood samples were collected by clinical physicians the following morning for further analysis. 008AS commercial kits (YZB 3632-40-2008, Shanghai Kehua Bioengineering Co., Ltd., Shanghai, China) were utilized to measure the levels of glucose, triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). SUA levels were measured using an automated biochemical analyzer, especially the Cobas C501 (ROCHE, Basel, Switzerland), through enzyme colorimetry.

Statistical Analyses

Categorical variables were presented as N (percentage), whereas continuous variables were expressed as mean \pm standard deviation (SD). To assess the differences between groups, we utilized the *t*-test for continuous variables and the chi-square test for categorical variables. The Mann-Whitney U test was used to assess the difference in serum uric acid levels between genotypes. Logistic regression analysis was employed to investigate the relationship between rs6068816 and hyperuricemia. Additionally, we applied multifactor dimensionality reduction (MDR) analysis to evaluate the potential interaction of rs6068816 and BMI. The statistical analyses were conducted using IBM's SPSS software version 21.0 (SPSS, Armonk, NY, USA), along with MDR 3.0.2 software (computational Genetics Laboratory of the University of Pennsylvania, Philadelphia, PA, USA). *p* values less than 0.05 were considered statistically significant.

Results

Basic Characteristics of Study Participants

The Demographic, anthropometric, and metabolic characteristics are displayed in Table 1. BMI, uric acid, triglyceride, total cholesterol, and high-density lipoprotein

Table 1. Comparison of demographic, anthropometric, and biochemical traits between the control group and the hyperuricemia group.

Variables	Control group (n = 130)	Hyperuricemia group (n = 130)	χ^2/t	<i>p</i> value
Male (n, %)	90 (69.2)	90 (69.2)	0.000	1.000
Age (years)	47.44 ± 19.54	47.09 ± 19.52	0.146	0.884
Educational level (n, %)			1.004	0.605
Elementary school or below	48 (36.9)	43 (33.1)		
Junior high school	52 (40.0)	60 (46.2)		
High school or above	30 (23.1)	27 (20.8)		
Marital status (n, %)			2.049	0.359
Unmarried	15 (11.5)	11 (8.5)		
Married	106 (81.5)	114 (87.7)		
Divorced/widowed	9 (6.9)	5 (3.8)		
Occupation (n, %)			0.021	0.990
Worker	34 (26.2)	33 (25.4)		
Famer	83 (63.8)	84 (64.6)		
Functionary	13 (10.0)	13 (10.0)		
SUA	200.10 ± 73.60	500.82 ± 228.00	14.313	<0.001*
BMI (Kg·m ⁻²)	23.40 ± 3.70	27.10 ± 4.30	7.561	<0.001*
TG (mmol·L ⁻¹)	1.17 ± 0.77	3.02 ± 2.34	8.536	<0.001*
TC (mmol·L ⁻¹)	4.25 ± 0.95	4.98 ± 1.33	5.088	<0.001*
HDL (mmol·L ⁻¹)	1.37 ± 0.29	1.22 ± 0.28	4.363	<0.001*
LDL (mmol·L ⁻¹)	2.36 ± 0.71	2.43 ± 0.85	0.702	0.483

Note: BMI, body mass index; SUA, serum uric acid; TG, triglyceride; TC, total cholesterol; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Asterisk denotes *p* values < 0.05.

Table 2. The frequency distribution of rs6068816 genotypes in patients with hyperuricemia and the control group.

SNP	Genotypes/Alleles	Control (n = 130)	Case (n = 130)	OR (95% CI)	<i>p</i>
rs6068816	TT	27	11	Reference	
	CT	63	64	2.494 (1.140–5.454)	0.020*
	CC	40	55	3.375 (1.500–7.593)	0.003*
TT vs CT+CC	TT	27	11	Reference	
	CT+CC	103	119	2.836 (1.341–5.998)	0.005*
TT+CT vs CC	TT+CT	90	75	Reference	
	CC	40	55	1.650 (0.991–2.747)	0.053
Allele	T	117	86	Reference	
	C	143	174	1.655 (1.160–2.362)	0.005*

Note: Asterisk indicates a *p* value < 0.05.

were significantly different between the case and control groups (*p* < 0.001). There were no significant differences in terms of gender, age, educational attainment, marital status, occupation, fasting blood glucose levels, or low-density lipoprotein (*p* > 0.05).

Genotyping Results of rs6068816

The genotyping results for rs6068816 are displayed in Table 2. The distribution of genotypes for rs6068816 exhibited conformity with the principles of Hardy-Weinberg equilibrium (*p* = 0.672). Compared with genotype TT, patients with hyperuricemia had a higher frequency of genotype CT (OR: 2.494, 95% CI: 1.140–5.454, *p* = 0.020) and

CC (OR: 3.375, 95% CI: 1.500–7.593, *p* = 0.003). The frequency of allele C was higher than allele T in the hyperuricemia group (OR: 1.655, 95% CI: 1.160–2.362, *p* = 0.005). In the dominant model of allele C, the frequency of genotype CT+CC in the case group was higher than that of genotype TT (OR: 2.836, 95% CI: 1.341–5.998, *p* = 0.005). There was no significant difference between the genotype TT+CT and CC (*p* = 0.053).

Comparison of Serum Urine Acid Level between Genotypes of rs6068816

The mean serum uric acid level was 390.3, 347.0, and 262.3 μmol/L for genotype CC, CT, and TT, respectively

Table 3. The association between CYP24A1 genotypes and hyperuricemia risk.

Models	Variables		OR (95% CI)	p
Model 1	rs6068816	TT	Reference	
		CT	2.667 (0.934–7.618)	0.067
		CC	5.061 (1.582–16.195)	0.006*
	BMI		6.756 (3.140–14.535)	<0.001*
Model 2	rs6068816	TT	Reference	
		CT	1.244 (0.249–6.218)	0.790
		CC	1.107 (0.216–5.678)	0.903
	BMI		1.749 (0.325–9.411)	0.515
rs6068816*BMI	TT*BMI	Reference		
	CT*BMI	3.025 (0.423–21.634)	0.270	
	CC*BMI	11.308 (1.420–90.049)	0.022*	

Note: In model 1, rs6068816 and BMI were included. In model 2, rs6068816, BMI and rs6068816 BMI were included. BMI was a categorical variable classified as below 24 kg/m² or above. The asterisk indicates p value < 0.05.

(Fig. 1). The mean serum uric acid level was significantly lower in individuals with the TT genotype compared to those with the CC genotype ($p = 0.001$) and CT genotype ($p = 0.009$). However, there were no significant differences between the CT and CC genotypes ($p = 0.456$).

compared with genotype TT (OR: 5.061, 95% CI: 1.582–16.195, $p = 0.006$). Furthermore, rs6068816 had a significant interaction with BMI in model 2. Compared with genotype TT BMI, CC BMI displayed a higher risk of hyperuricemia (OR: 11.308, 95% CI: 1.420–90.049, $p = 0.022$).

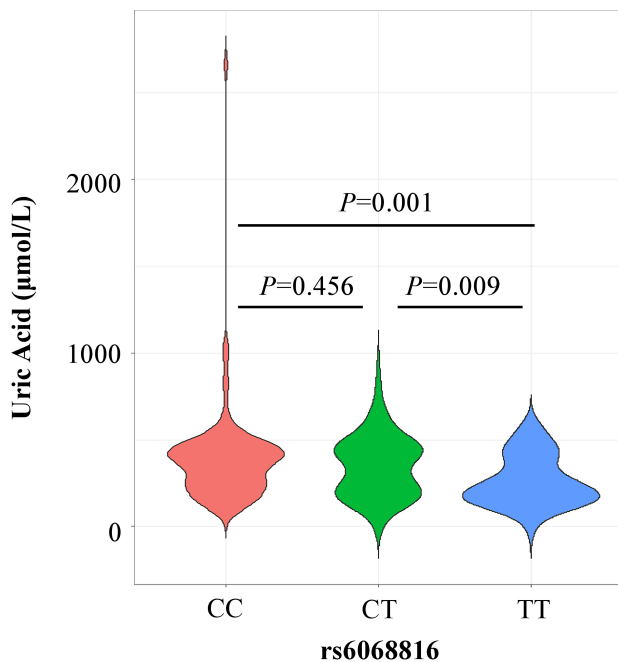


Fig. 1. Comparison of serum urine acid level between genotypes of rs6068816. The Mann-Whitney U test was used to compare the differences between genotypes.

Association of rs6068816 with Hyperuricemia

The findings from the logistic regression model can be observed in Table 3. Results for model 1 indicate that people with genotype CC had a higher risk of hyperuricemia

Table 4. The results of the interaction model by multifactor dimensionality reduction.

Model	CVC	Testing balanced accuracy	p
1 BMI	10/10	0.685	0.050
2 rs6068816, BMI	10/10	0.696	0.044*

Note: BMI was dichotomous with a cutoff value of 24 kg/m². Asterisk indicates the p value < 0.05. CVC, cross-validation consistency.

Interaction of rs6068816 and BMI

As shown in Table 4, MDR analysis was used to further evaluate the interaction between rs6068816 and BMI. The results indicated that rs6068816 and BMI displayed a significant interaction effect for the prediction of hyperuricemia. The optimal interaction model included rs6068816 and BMI, exhibiting a cross-validation consistency score of 10/10 and a balanced accuracy rate of 0.696 in testing ($p = 0.044$).

Discussion

In this study, we analyzed the association between rs6068816 and hyperuricemia. The results indicated that allele C of rs6068816 conveyed an increased risk for hyperuricemia. Genotype CC of rs6068816 was associated with higher susceptibility to hyperuricemia. Furthermore, rs6068816 displayed a significant multiplicative interaction with BMI for the prediction of hyperuricemia risk. Thus, overweight people with genotype CC may face a higher risk of hyperuricemia.

Abnormal Levels of Vitamin D and Hyperuricemia Risk

Abnormal vitamin D levels, a crucial fat-soluble nutrient vital for the body's functioning, have been linked to an elevated likelihood of hyperuricemia [17]. In a study by Y. Han *et al.* [18] involving 18,596 individuals aged 18 and older, serum 25(OH)D₃ was negatively correlated with hyperuricemia. However, a study conducted on 9920 Chinese adults revealed that there was a positive correlation between levels of SUA and 25(OH)D₃. Additionally, it was observed that for every increase of 10 nmol/L in 25(OH)D₃, the incidence of hyperuricemia increased by approximately 9.4% [19]. In addition, a systematic review and meta-analysis conducted on 32 studies aimed to explore the correlation between vitamin D and uric acid levels in adults. The findings suggested that elevated serum uric acid levels may be linked to higher concentrations of 25(OH)D₃, while insufficiency of vitamin D is associated with hyperuricemia. One possible reason is that genetic factors could influence both vitamin D and SUA levels. Gene polymorphisms clearly play a significant role in vitamin D and SUA levels [20]. *CYP24A1* gene variations have been significantly associated with 25(OH)D₃ levels. Serum 25(OH)D₃ functions as a clinical indicator for assessing vitamin D levels, being the predominant metabolite of vitamin D found in circulation. Therefore, there may be an association between *CYP24A1* gene variations and hyperuricemia.

Association between Polymorphism of CYP24A1 Gene and Hyperuricemia

CYP24A1 is involved in the inactivation of the vitamin D functional metabolite. Results of several studies suggest that people with abnormal vitamin D levels are likely to face an increased risk of metabolic disease. Chai *et al.* [21] found that the *CYP24A1* gene polymorphism may contribute to the risk of colorectal cancer development by increasing the barrier to vitamin D absorption. A case-control study designed by Qian *et al.* [22] suggested that the rs6068816 variant significantly increased the risk of coronary heart disease in various genetic models. In addition, variation in the *CYP24A1* gene may be associated with vitamin D-related metabolic disorders such as hyperuricemia, as suggested by the association between rs6068816 and hyperuricemia found in the present study. The SNP rs6068816 is located in the exon of the *CYP24A1* gene as a synonymous variant. Because the *CYP24A1* gene has a significant impact on the regulation of vitamin D activity and variation in rs6068816 might lead to aberrant expression of the *CYP24A1* gene by code preference, which then may have an impact on the vitamin D level, and thus contribute to the development of hyperuricemia. Further research is required to uncover the underlying mechanism linking rs6068816 and hyperuricemia.

Interaction between rs6068816 and BMI on Hyperuricemia

The presence of elevated levels of uric acid in the blood is determined by a combination of genetic and environmental factors [23]. Susceptibility based on individual genetic factors may increase under the influence of certain environmental factors. In this study, we identified an interaction between rs6068816 and BMI that significantly increased the risk of hyperuricemia. However, the potential mechanism of this interaction remains obscure. According to the literature, mutation in the *CYP24A1* gene and obesity are both risk factors for hyperuricemia, and the effects of both may be mediated through abnormal vitamin D metabolism [24,25]. In particular, the *CYP24A1* gene is a vitamin D regulatory gene, which catalyzes the conversion from its hormonal form 1,25-(OH)₂D₃ into 24-hydroxylated products, potentially leading to reduced uric acid excretion [26]. Previous studies have suggested specific molecular mechanisms. It has been suggested that the mild uric acid-lowering effect of vitamin D is mediated by the suppression of parathyroid hormone (PTH); PTH is known to downregulate the adenosine-triphosphate (ATP)-binding cassette transporter G2 (ABCG2) in the kidneys, leading to a reduction in the renal clearance of uric acid [27]. Moreover, vitamin D is fat-soluble and will be diluted as fat accumulates in the body, and reduced vitamin D levels might contribute to the incidence of hyperuricemia. However, further research is needed to explore the biological mechanisms and to better explain the identified interaction.

In summary, we found that rs6068816 in the *CYP24A1* gene was significantly associated with hyperuricemia. The presence of allele C in rs6068816 increases the susceptibility to hyperuricemia, and its association with BMI can be used as a predictor for the risk of developing hyperuricemia. These findings could potentially provide novel insights into the prevention and treatment of hyperuricemia.

Conclusions

rs6068816 was found to be associated with hyperuricemia in the Chinese population. Future studies may explore this association, in combination with additional epidemiological indicators, to improve the prediction of hyperuricemia risk. Further investigations with larger sample sizes, as well as mechanistic studies, are required to verify the conclusions of this study.

Availability of Data and Materials

The authors confirm that all data generated or analysed during this study are included in this published article. Furthermore, primary and secondary sources and data supporting the findings of this study were all publicly available at the time of submission.

Author Contributions

JHSG wrote the manuscript and performed the statistical analysis. JHSG, WJZ, XDZ, YYZ, RX and LLX contributed to data collection. LLX, YYZ and RX examined the document and explained the information. GQL was responsible for study design, management and coordination of the planning and execution of the study activities, as well as providing financial support for the study. All authors contributed significantly to editorial changes of important content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The research was conducted following the guidelines stated in the Declaration of Helsinki, and approved by the Life Science Ethics Committee of Zhengzhou University (Ethics Approval Number: KY-2020-0047). And written informed consent was obtained from all participants.

Acknowledgment

The colleagues who actively contributed to this case-control study are sincerely acknowledged by the author. Gratitude is extended to all the patients who willingly took part in this research.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Bardin T, Richette P. Definition of hyperuricemia and gouty conditions. *Current Opinion in Rheumatology*. 2014; 26: 186–191.
- [2] Dong X, Zhang H, Wang F, Liu X, Yang K, Tu R, *et al*. Epidemiology and prevalence of hyperuricemia among men and women in Chinese rural population: The Henan Rural Cohort Study. *Modern Rheumatology*. 2020; 30: 910–920.
- [3] Li C, Hsieh MC, Chang SJ. Metabolic syndrome, diabetes, and hyperuricemia. *Current Opinion in Rheumatology*. 2013; 25: 210–216.
- [4] Mallat SG, Al Kattar S, Tanios BY, Jurjus A. Hyperuricemia, Hypertension, and Chronic Kidney Disease: an Emerging Association. *Current Hypertension Reports*. 2016; 18: 74.
- [5] Fatima T, Iftikhar S, Qureshi IH. Association between Hyperuricemia and Ischemic Stroke: A Case-Control Study. *Journal of the College of Physicians and Surgeons–Pakistan*. 2020; 30: 853–856.
- [6] Borghi C, Agabiti-Rosei E, Johnson RJ, Kielstein JT, Lurbe E, Mancia G, *et al*. Hyperuricaemia and gout in cardiovascular, metabolic and kidney disease. *European Journal of Internal Medicine*. 2020; 80: 1–11.
- [7] Yokose C, McCormick N, Choi HK. The role of diet in hyperuricemia and gout. *Current Opinion in Rheumatology*. 2021; 33: 135–144.
- [8] Zhang YY, Qiu HB, Tian JW. Association Between Vitamin D and Hyperuricemia Among Adults in the United States. *Frontiers in Nutrition*. 2020; 7: 592777.
- [9] Nielsen SM, Bartels EM, Henriksen M, Wæhrens EE, Gudberg H, Bliddal H, *et al*. Weight loss for overweight and obese individuals with gout: a systematic review of longitudinal studies. *Annals of the Rheumatic Diseases*. 2017; 76: 1870–1882.
- [10] Yu S, Li X, Yu F, Mao Z, Wang Y, Xue Y, *et al*. New evidence for associations between vitamin D receptor polymorphism and obesity: case-control and family-based studies. *Journal of Human Genetics*. 2020; 65: 281–285.
- [11] Welsh J. Function of the vitamin D endocrine system in mammary gland and breast cancer. *Molecular and Cellular Endocrinology*. 2017; 453: 88–95.
- [12] Wang Y, Wang O, Li W, Ma L, Ping F, Chen L, *et al*. Variants in Vitamin D Binding Protein Gene Are Associated With Gestational Diabetes Mellitus. *Medicine*. 2015; 94: e1693.
- [13] Martinaityte I, Jorde R, Emaus N, Eggen AE, Joakimsen RM, Kamycheva E. Bone mineral density is associated with vitamin D related rs6013897 and estrogen receptor polymorphism rs4870044: The Tromsø study. *PLoS ONE*. 2017; 12: e0173045.
- [14] Ye X, Jia J, Zhang N, Ding H, Zhan Y. Associations of genetic polymorphisms of the vitamin D pathway with blood pressure in a Han Chinese population. *Clinical and Experimental Hypertension*. 2019; 41: 460–465.
- [15] Yi C, Huang C, Wang H, Wang C, Dong L, Gu X, *et al*. Association study between CYP24A1 gene polymorphisms and cancer risk. *Pathology, Research and Practice*. 2020; 216: 152735.
- [16] Zhou BF. Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults—study on optimal cut-off points of body mass index and waist circumference in Chinese adults. *Biomedical and Environmental Sciences*. 2002; 15: 83–96.
- [17] Christakos S, Dhawan P, Verstuyf A, Verlinden L, Carmeliet G. Vitamin D: Metabolism, Molecular Mechanism of Action, and Pleiotropic Effects. *Physiological Reviews*. 2016; 96: 365–408.
- [18] Han Y, Han K, Zhang Y, Zeng X. Serum 25-hydroxyvitamin D might be negatively associated with hyperuricemia in U.S. adults: an analysis of the National Health and Nutrition Examination Survey 2007–2014. *Journal of Endocrinological Investigation*. 2022; 45: 719–729.
- [19] Chen Y, Cheng J, Chen Y, Wang N, Xia F, Chen C, *et al*. Association between serum vitamin D and uric acid in the eastern Chinese population: a population-based cross-sectional study. *BMC Endocrine Disorders*. 2020; 20: 79.
- [20] Isnwardana R, Bijukchhe S, Thadanipon K, Ingsathit A, Thakkinstian A. Association Between Vitamin D and Uric Acid in Adults: A Systematic Review and Meta-Analysis. *Hormone and Metabolic Research*. 2020; 52: 732–741.
- [21] Chai L, Ni J, Ni X, Zhang N, Liu Y, Ji Z, *et al*. Association of CYP24A1 gene polymorphism with colorectal cancer in the Jiamusi population. *PLoS ONE*. 2021; 16: e0253474.
- [22] Qian P, Cao X, Xu X, Duan M, Zhang Q, Huang G. Contribution of CYP24A1 variants in coronary heart disease among the Chinese population. *Lipids in Health and Disease*. 2020; 19: 181.
- [23] Cheng ST, Wu S, Su CW, Teng MS, Hsu LA, Ko YL. Association of ABCG2 rs2231142-A allele and serum uric acid levels in male and obese individuals in a Han Taiwanese population. *Journal of the Formosan Medical Association*. 2017; 116: 18–23.
- [24] Matsuura F, Yamashita S, Nakamura T, Nishida M, Nozaki S, Funahashi T, *et al*. Effect of visceral fat accumulation on uric

acid metabolism in male obese subjects: visceral fat obesity is linked more closely to overproduction of uric acid than subcutaneous fat obesity. *Metabolism: Clinical and Experimental*. 1998; 47: 929–933.

- [25] Ali N, Perveen R, Rahman S, Mahmood S, Rahman S, Islam S, *et al*. Prevalence of hyperuricemia and the relationship between serum uric acid and obesity: A study on Bangladeshi adults. *PLoS ONE*. 2018; 13: e0206850.
- [26] Meyer MB, Pike JW. Mechanistic homeostasis of vitamin D metabolism in the kidney through reciprocal modulation of Cyp27b1 and Cyp24a1 expression. *The Journal of Steroid Biochemistry and Molecular Biology*. 2020; 196: 105500.
- [27] Sugimoto R, Watanabe H, Ikegami K, Enoki Y, Imafuku T, Sakaguchi Y, *et al*. Down-regulation of ABCG2, a urate exporter, by parathyroid hormone enhances urate accumulation in secondary hyperparathyroidism. *Kidney International*. 2017; 91: 658–670.