Associations between Serum Vitamins and Serum Uric Acid in a Population of Shenyang, China

Yashu Liu1,2, Yang Xia1,2, Qijun Wu1,2, Qing Chang1,2 and Yuhong Zhao1,2,*

1 Department of Clinical Epidemiology, Shengjing Hospital of China Medical University, Shenyang, China
2 Clinical Research Center, Shengjing Hospital of China Medical University, Shenyang, China

(Received August 26, 2020)

Summary Previous studies have demonstrated that serum vitamins are associated with serum uric acid (SUA) level. However, no study has comprehensively investigated whether various serum vitamins are associated with SUA level in a general population. Thus, a cross-sectional study was designed to explore the associations between SUA level and serum vitamins. The data of this study for SUA levels were collected from participants aged ≥18 y. Serum vitamin and other baseline information, including age and body mass index, was determined. Moreover, associations between SUA level and serum vitamins were explored using analysis of covariance. Higher levels of SUA were significantly associated with a higher level of serum vitamins A, B9 and B5 (p<0.05). Higher level of SUA were associated with a lower level of serum vitamins C, and D2 (p<0.05). No significant associations were found between vitamins C, and D2 and SUA levels after adjustment. Study results suggested that serum vitamins A, B9 and B5 were positively associated, whereas serum vitamins C, and D2 were inversely associated with SUA levels.

Key Words serum vitamins, serum uric acid, cross-sectional study, Chinese population, comprehensively investigation

Uric acid is the final product of purine or nucleotide metabolism. High levels of serum uric acid (SUA) are the main prerequisite for gout (1, 2). Previous study results suggested a globally rising trajectory of gout burden between 1990 and 2017 (3). The overall prevalence of hyperuricemia in the United States was 14.6% (4). A high prevalence of SUA has also been detected in China (5) and Pakistan (6). Hyperuricemia has been shown to be associated with a high risk of hypertension (7), peripheral and coronary arterial disease (8, 9), cardiovascular disease (10), diabetes mellitus (11), and chronic kidney disease (12) in a general population. Thus, high SUA level and its potential health consequences are now considered to be an important public health concern. It is thus necessary to be able to control the development of SUA level.

Among the potentially useful protective factors that impact hyperuricemia and gout, vitamins are essential micronutrients for humans. Evidence has suggested that concentrations of uric acid are significantly and positively associated with concentrations of vitamin A and inversely with concentrations of beta-carotene (13). In addition, meta-analysis has suggested that patients with both vitamin D insufficiency and deficiency have a significantly higher level of SUA compared to individuals with normal vitamin D levels (14). Population-based data indicated that vitamin C intake is inversely associated with SUA concentrations (15). Thus, it was hypothesized that serum vitamins may have different effects on SUA level.

A cross-sectional study among Chinese postmenopausal women suggested that participants with vitamin D insufficiency are more likely to have elevated uric acid compared to those without. This association between vitamin D was not significant among premenopausal women. It is worth noting that diet patterns among Chinese individuals are different from other countries. Chinese have a higher intake of refined rice, which has lost some vitamins (16). The prevalence of hyperuricemia is 10.9% in a rural Northeast Chinese population and their special living habits are related to hyperuricemia (17). However, no study to date has comprehensively investigated whether various serum vitamins, such as vitamins K and E, are associated with SUA levels in a general population, especially in Northeast China. Thus, a cross-sectional study was designed to explore the associations between various serum vitamins and SUA levels in Northeast Chinese adults.

MATERIALS AND METHODS

Study population. A total of 166 participants were recruited from Northeast China. This cross-sectional study included 113 health population without gout in urban city who did not attend to outdoor farm work. These subjects had been tested for serum vitamins and uric acid concentrations. The participants received health examinations and were asked to answer questionnaires that included questions related to their lifestyle. Written informed consent was obtained from all participants. This study was conducted according to the guidelines laid down in the Declaration of Helsinki. The
| Variable                                      | Quartile 1                        | Quartile 2                        | Quartile 3                        | Quartile 4                        |
|----------------------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|
| Number                                       | 33                                | 33                                | 32                                | 33                                |
| Uric acid (range, μmol/L)                    | 145.8–268.1                       | 268.9–318.2                       | 318.3–380.8                       | 383.0–632.3                       |
| Uric acid (range, mg/dL)                     | 2.5–4.5                           | 4.5–5.3                           | 5.4–6.4                           | 6.4–10.6                          |
| Age (y)                                      | 32.4 (27.9, 36.8)                 | 35.0 (30.6, 39.5)                 | 29.5 (25.0, 34.0)                 | 26.6 (22.1, 31.0)                 |
| Gender (male %)                              | 0                                 | 11.9                              | 23.8                              | 64.3                              |
| BMI (kg/m²)                                  | 21.1 (20.0, 22.3)                 | 21.4 (20.2, 22.6)                 | 22.8 (21.6, 24.0)                 | 24.3 (23.1, 25.5)*                |
| eGFR (mL/min·1.73 m²)                        | 96.2 (92.6, 99.8)                 | 94.7 (91.1, 98.3)                 | 96.1 (92.4, 99.7)                 | 98.4 (94.8, 102.0)                |
| Total energy intake (kcal/d)                 | 2318.2 (2018.7, 2617.7)           | 2259.0 (1954.8, 2563.2)           | 2348.3 (2044.1, 2052.5)           | 2568.6 (2269.1, 2868.1)           |
| Vegetables intake (g/d)                      | 190.0 (148.7, 231.3)              | 167.7 (126.4, 209.0)              | 169.9 (127.9, 211.87)             | 208.1 (166.8, 249.4)              |
| Fruit intake (g/d)                           | 213.4 (169.5, 257.3)              | 206.5 (162.6, 250.3)              | 202.0 (157.5, 246.6)              | 227.0 (183.1, 270.9)              |
| Animal food intake (g/d)                     | 101.7 (81.9, 121.6)               | 108.5 (88.7, 128.4)               | 128.9 (108.7, 149.0)              | 121.6 (101.7, 141.4)              |
| Vitamin A (ng/mL)                            | 565.9 (489.9, 641.9)              | 588.8 (512.8, 664.8)              | 651.6 (574.4, 728.8)              | 696.3 (620.2, 772.3)              |
| Vitamin B1 (ng/mL)                           | 1.1 (0.9, 1.3)                    | 1.3 (1.2, 1.5)                    | 1.1 (0.9, 1.2)                    | 1.3 (1.1, 1.4)                    |
| Vitamin B2 (ng/mL)                           | 4.7 (0.6, 8.9)                    | 9.6 (5.4, 13.8)                   | 4.2 (–0.1, 8.4)                   | 5.4 (1.2, 9.5)                    |
| Vitamin B3 (ng/mL)                           | 29.4 (20.6, 38.2)                 | 32.6 (23.8, 41.4)                 | 30.1 (21.2, 39.0)                 | 34.6 (25.8, 43.3)                 |
| Vitamin B5 (ng/mL)                           | 27.1 (23.7, 30.4)                 | 33.8 (30.4, 37.2)                 | 32.9 (29.5, 36.4)                 | 35.4 (32.0, 38.7)                 |
| Vitamin B6 (ng/mL)                           | 2.2 (1.8, 2.6)                    | 2.3 (1.9, 2.7)                    | 2.1 (1.7, 2.4)                    | 2.6 (2.3, 3.0)                    |
| Vitamin B7 (ng/mL)                           | 2.5 (0.4, 4.5)                    | 0.5 (–1.5, 2.6)                   | 0.9 (–1.1, 3.0)                   | 1.9 (–0.1, 3.9)                   |
| Vitamin B9 (ng/mL)                           | 11.0 (8.6, 13.3)                  | 13.2 (10.8, 15.5)                 | 11.5 (9.1, 13.8)                  | 8.8 (6.5, 11.1)                   |
| Vitamin B12 (ng/mL)                          | 0.2 (0.1, 0.3)                    | 0.2 (0.1, 0.3)                    | 0.2 (0.1, 0.2)                    | 0.2 (0.2, 0.3)                    |
| Vitamin C (μg/mL)                            | 11.9 (10.1, 13.8)                 | 9.6 (7.8, 11.5)                   | 10.2 (8.4, 12.1)                  | 8.5 (6.7, 10.4)                   |
| Vitamin D2 (ng/mL)                           | 2.6 (2.0, 3.1)                    | 2.7 (2.2, 3.3)                    | 2.4 (1.8, 2.9)                    | 1.8 (1.2, 2.3)                    |
| Vitamin D3 (ng/mL)                           | 16.2 (11.9, 20.5)                 | 20.4 (16.1, 24.7)                 | 18.8 (14.4, 23.2)                 | 16.0 (11.7, 20.3)                 |
| Vitamin E (μg/mL)                            | 11.2 (8.7, 13.7)                  | 11.8 (9.3, 14.3)                  | 13.0 (10.4, 15.5)                 | 11.3 (8.8, 13.8)                  |
| Vitamin K (ng/mL)                            | 0.6 (0.4, 0.8)                    | 0.3 (0.1, 0.5)                    | 0.4 (0.2, 0.7)                    | 0.2 (0.0, 0.4)*                   |
| Smoking status (Smoker %)                    | 0                                 | 25.0                              | 37.5                              | 37.5                              |
| Drinking status (Drinker %)                  | 0                                 | 50.0                              | 16.7                              | 33.3                              |

BMI, body mass index; eGFR, estimated glomerular filtration rate.

1 All values are expressed as mean±standard deviation.

*p<0.05, compared with quartile 1.

**p<0.05, compared with quartile 2.
study was approved by the Ethics Committee of China Medical University (2017PS190K). Written informed consent was obtained from all participants.

Assessment of SUA levels and other variables. Venous blood samples were obtained from all participants after an overnight fast (at least 12 h). All blood sample was test in medical laboratory center of Shengjing Hospital. The venous blood sample was collection in separation gel tube. Then, the serum was collected after centrifuging with 3,500 r/min, 10 min. The serum sample was used to test the concentration of serum vitamin and SUA. The principal study variables included concentrations of SUA and vitamins A (retinol), B1, B2, B3, B5, B6, B7, B9, B12, C, D2 (25[OH]D2), D3 (25[OH]D3), E, and K. All of the above vitamins were quantified using a mass spectrometer (API3200MD). Blood sample uric acid levels were analyzed using the HX_AU5400 or HX_AU5800 Automated Biochemical Analyzer.

Assessment of covariates. All participants received health examinations and were interviewed using a questionnaire to obtain information about their demographic characteristics, lifestyle, dietary habits, and other exposures. Total energy intake (kcal/d) was obtained from information provided during a semiquantitative food frequency questionnaire (FFQ), which included a survey of 110 foods items. Vegetables and fruits intake were also obtained from the FFQ. Intake of vegetables summarized the intake of Chinese cabbage, cabbage, oilseed rape, spinach, tomatoes and its products, pumpkin, cucumber, wax gourd, celery, eggplant, broccoli, cauliflower, carrot and other radish, pepper and chili, edible fungus, Chinese chives, onion, garlic, sprout, sea-plant, lotus root, red dates, Chinese onion, and garlic. Fruits intake summarized the intake of apple, pear, orange, banana, watermelon, peach, pineapple, kiwi fruit, grape, strawberry, and other fruits. In addition, drinking status was defined by a self-reported questionnaire. Participants was identified to drinker by the frequency of drinking any alcohol products, which was more than once per week and lasted more than 6 mo. Body mass index (BMI, kg/m²) was computed as the ratio of weight (kg) to height squared (m²). All participants were measured without wearing shoes. Body weight was obtained using Body Composition Analyzers and height measurements were recorded to the nearest 0.1 cm. Estimate glomerular filtration rate (eGFR) was calculated using the “Xiangya equation” (18). Smoking status was divide into non-smoker and smoker. Drinking status was divide into non-drinker and drinker.

Statistical analyses. Descriptive data were represented as the mean±standard deviation (SD) for continuous variables. Categorical variables were represented as numbers of subjects and percentages. Based on the distribution of SUA levels, subjects were divided into equal quartiles, which divided all participants into four group according <25%, 25–50%, 50–75%, >75% of SUA level. Analysis of covariance was used to assess the differences between SUA categories and serum vitamin after adjustment for covariates. Age, sex, BMI, and total energy intake were adjusted in Model 1. Additionally, Model 2 adjusted for estimated glomerular filtration rate, urine pH, smoking status, and drinking status based on Model 1. The least square means (95% confidence intervals) of vitamins according to quartiles of SUA were also calculated using analysis of covariance. All statistical analyses were performed using the Statistical Analysis System 9.3 edition for Windows (SAS Institute Inc., Gary, NC, USA). All tests were two-tailed and p<0.05 was defined as statistically significant.

RESULTS

The average age of males was 28.07±10.72 y (range 18–70) and the average level of SUA was 411.95±80.86 μmol/L. A total of 89 females participated in the study, with an average age of 32.21±13.98 y (range 19–66, median 25) and average level of SUA of 287.53±63.53 μmol/L (Table 1 and Supplemental Online Material, Table S1).

The crude and adjusted association between quartiles of SUA levels and serum were presented in Table 2. Compared to participants with the lowest serum levels of SUA, the highest SUA levels participants are with a low levels of vitamin C, D2 and K level (p<0.05) and a high level of vitamins A and B5 (p<0.05) before adjusting for covariates. In the multivariate models, higher serum levels of SUA were significantly associated with a higher vitamins A, B9 and B5 level (p<0.05). However, associations between SUA and vitamins K, C, and D2 disappeared after adjusting for potential confounders. Similarly, associations between vitamins B1, B2, B3, B6, B7, B12, D3 and E and SUA levels were not significant.

DISCUSSION

In a cross-sectional study of a representative sample of Shenyang adults, concentrations of serums A, B9 and B5 were significantly and positively associated with SUA. Considering their role in various pathologies, identifying factors that contribute to elevated uric acid concentrations can yield new insights into therapeutic options for optimizing SUA level concentrations.

Results from the present study are in agreement with recently published evidence. In an analysis of data from a national survey of 14,542 adults conducted between 2001 and 2006 in the United States, concentrations of vitamin A were inversely associated with concentrations of SUA (13). Another study suggested that food fortification with vitamin A supplements may contribute to the high frequency of hyperuricemia in the U.S. population, whereas β-carotene intake may be beneficial against hyperuricemia (19).

There are several plausible biological explanations for the association between serum levels of vitamin A and concentrations of SUA (13, 19). First, xanthine oxidase, which converts retinol to retinoic acid and xanthines to SUA, provides a mechanistic explanation for changes in vitamin A concentrations that may impact concentrations of SUA (13). Second, a biological mechanism underlying the link between retinol and hyperuricemia is hypothesized to involve the action of xanthine oxidase shared by the SUA level production and retinol oxi-
Table 2. Serum vitamin levels according to the quartiles of serum uric acid.

| Vitamin | Level of serum uric acid | Quartile 1 | Quartile 2 | Quartile 3 | Quartile 4 | p for trend$^1$ |
|---------|-------------------------|------------|------------|------------|------------|-----------------|
|         |                         | Number of participants | 33          | 33          | 32          | 33              |
|         |                         | Uric acid (range, μmol/L) | 145.8–268.1 | 268.9–318.2 | 318.3–380.8 | 383.0–632.3    |
|         |                         | Uric acid (range, mg/dL)  | 2.5–4.5     | 4.5–5.3     | 5.4–6.4     | 6.4–10.6       |
|         | Vitamin A               | Crude (ng/mL) | 565.9 (489.9, 641.9) | 588.8 (512.8, 664.8) | 651.6 (574.4, 728.8) | 696.3 (620.2, 772.3) | <0.01 |
|         |                         | Model 1 (ng/mL) | 508.7 (426.8, 610.0) | 534.5 (458.9, 610.0) | 643.7 (574.0, 713.4) | 761.4 (684.6, 838.1) | <0.001 |
|         |                         | Model 2 (ng/mL) | 475.5 (386.6, 564.3) | 532.1 (452.7, 611.5) | 642.5 (567.0, 718.0) | 730.0 (651.7, 808.2) | <0.001 |
|         | Vitamin B1              | Crude (ng/mL) | 1.1 (0.9, 1.3) | 1.3 (1.2, 1.5) | 1.1 (0.9, 1.2) | 1.3 (1.1, 1.4) | 0.7 |
|         |                         | Model 1 (ng/mL) | 1.1 (0.9, 1.3) | 1.3 (1.1, 1.5) | 1.0 (0.9, 1.2) | 1.2 (1.0, 1.4) | 0.9 |
|         |                         | Model 2 (ng/mL) | 1.0 (0.8, 1.2) | 1.2 (1.0, 1.4) | 1.1 (0.9, 1.2) | 1.3 (1.1, 1.5) | 0.2 |
|         | Vitamin B2              | Crude (ng/mL) | 4.7 (0.6, 8.9) | 9.6 (5.4, 13.8) | 4.2 (−0.1, 8.4) | 5.4 (1.2, 9.5) | 0.7 |
|         |                         | Model 1 (ng/mL) | 4.1 (−1.2, 9.4) | 9.4 (4.5, 14.3) | 3.6 (−0.9, 8.1) | 5.4 (0.4, 10.3) | 0.9 |
|         |                         | Model 2 (ng/mL) | 4.6 (−1.6, 10.7) | 9.7 (4.2, 15.2) | 3.3 (−1.9, 8.5) | 5.4 (−0.1, 10.8) | 0.8 |
|         | Vitamin B3              | Crude (ng/mL) | 29.4 (20.6, 38.2) | 32.6 (23.8, 41.4) | 30.1 (21.2, 39.0) | 34.6 (25.8, 43.3) | 0.5 |
|         |                         | Model 1 (ng/mL) | 28.7 (17.9, 39.6) | 31.9 (21.9, 42.0) | 31.6 (22.3, 40.8) | 38.0 (27.8, 48.2) | 0.3 |
|         |                         | Model 2 (ng/mL) | 27.0 (15.1, 39.0) | 34.2 (23.5, 44.9) | 33.3 (23.1, 43.5) | 37.6 (27.0, 48.2) | 0.3 |
|         | Vitamin B5              | Crude (ng/mL) | 27.1 (23.7, 30.4) | 33.8 (30.4, 37.2) | 32.9 (29.5, 36.4) | 35.4 (32.0, 38.7) | <0.01 |
|         |                         | Model 1 (ng/mL) | 24.4 (20.6, 28.1) | 30.6 (27.1, 34.0) | 32.4 (29.2, 35.6) | 37.2 (33.7, 40.7) | <0.0001 |
|         |                         | Model 2 (ng/mL) | 23.2 (19.0, 27.4) | 30.0 (26.2, 33.7) | 32.6 (29.1, 36.2) | 36.8 (33.1, 40.4) | <0.0001 |
|         | Vitamin B6              | Crude (ng/mL) | 2.2 (1.8, 2.6) | 2.3 (1.9, 2.7) | 2.1 (1.7, 2.4) | 2.6 (2.3, 3.0) | 0.2 |
|         |                         | Model 1 (ng/mL) | 2.1 (1.6, 2.5) | 2.2 (1.8, 2.6) | 2.0 (1.6, 2.4) | 2.7 (2.3, 3.1) | 0.1 |
|         |                         | Model 2 (ng/mL) | 2.0 (1.6, 2.5) | 2.2 (1.8, 2.6) | 2.1 (1.7, 2.5) | 2.6 (2.2, 3.0) | 0.2 |
|         | Vitamin B7              | Crude (ng/mL) | 2.5 (0.4, 4.5) | 0.5 (−1.5, 2.6) | 0.9 (−1.1, 3.0) | 1.9 (−0.1, 3.9) | 0.8 |
|         |                         | Model 1 (ng/mL) | 0.7 (−1.8, 3.2) | −0.6 (−2.9, 1.7) | 0.5 (−1.6, 2.6) | 3.2 (0.9, 5.5) | 0.2 |
|         |                         | Model 2 (ng/mL) | 0.8 (−1.9, 3.4) | −0.5 (−2.8, 1.9) | 0.6 (−1.7, 2.8) | 3.1 (0.7, 5.4) | 0.2 |
|         | Vitamin B9              | Crude (ng/mL) | 11.0 (8.6, 13.3) | 13.2 (10.8, 15.5) | 11.5 (9.1, 13.8) | 8.8 (6.5, 11.1) | 0.1 |
|         |                         | Model 1 (ng/mL) | 7.6 (4.9, 10.3) | 10.4 (7.9, 12.9) | 10.7 (8.4, 13.0) | 11.7 (9.2, 14.2) | 0.1 |
|         |                         | Model 2 (ng/mL) | 5.9 (3.0, 8.8) | 11.0 (8.5, 13.6) | 10.9 (8.5, 13.4) | 11.4 (8.9, 14.0) | <0.05 |
### Table 2. (Continued)

| Vitamin       | Level of serum uric acid |          |          |          |          | \( p \) for trend $^1$ |
|---------------|--------------------------|----------|----------|----------|----------|------------------------|
|               | Quartile 1               | Quartile 2 | Quartile 3 | Quartile 4 |
| B12 Crude     | 0.2 (0.1, 0.3)           | 0.2 (0.1, 0.3) | 0.2 (0.1, 0.2) | 0.2 (0.2, 0.3) | 0.3 |
| B12 Model 1$^1$| 0.1 (0.1, 0.2)           | 0.2 (0.1, 0.2) | 0.2 (0.1, 0.2) | 0.3 (0.2, 0.4) | 0.1 |
| B12 Model 2$^4$| 0.2 (0.0, 0.5)           | 0.2 (0.0, 0.3) | 0.5 (0.3, 0.6) | 0.3 (0.1, 0.5) | 0.3 |
| C Crude       | 11.9 (10.1, 13.8)        | 9.6 (7.8, 11.5) | 10.2 (8.4, 12.1) | 8.5 (6.7, 10.4) | <0.05 |
| C Model 1$^3$ | 9.6 (7.4, 11.8)          | 8.0 (6.0, 10.0) | 9.3 (7.5, 11.2) | 9.9 (7.9, 12.0) | 0.7 |
| C Model 2$^4$ | 9.7 (7.2, 12.2)          | 8.0 (5.8, 10.2) | 10.2 (8.1, 12.3) | 10.2 (8.0, 12.4) | 0.5 |
| D2 Crude      | 2.6 (2.0, 3.1)           | 2.7 (2.2, 3.3) | 2.4 (1.8, 2.9) | 1.8 (1.2, 2.3) | <0.05 |
| D2 Model 1$^3$| 2.0 (1.3, 2.7)           | 2.4 (1.7, 3.0) | 2.2 (1.6, 2.8) | 2.3 (1.6, 2.8) | 0.7 |
| D2 Model 2$^4$| 2.0 (1.3, 2.7)           | 2.3 (1.7, 3.0) | 2.2 (1.6, 2.8) | 2.3 (1.7, 2.9) | 0.7 |
| D3 Crude      | 16.2 (11.9, 20.5)        | 20.4 (16.1, 24.7) | 18.8 (14.4, 23.2) | 16.0 (11.7, 20.3) | 0.8 |
| D3 Model 1$^3$| 14.9 (10.5, 19.3)        | 16.7 (12.6, 20.8) | 19.0 (15.3, 22.8) | 18.0 (13.9, 22.1) | 0.3 |
| D3 Model 2$^4$| 14.8 (10.4, 19.3)        | 17.1 (13.1, 21.0) | 17.1 (13.3, 20.9) | 16.6 (12.7, 20.5) | 0.6 |
| E Crude       | 11.2 (8.7, 13.7)         | 11.8 (9.3, 14.3) | 13.0 (10.4, 15.5) | 11.3 (8.8, 13.8) | 0.8 |
| E Model 1$^3$ | 9.2 (6.3, 12.1)          | 9.7 (7.0, 12.4) | 12.5 (10.0, 15.0) | 13.1 (10.4, 15.9) | <0.05 |
| E Model 2$^4$ | 10.8 (7.7, 13.8)         | 8.9 (6.2, 11.6) | 12.2 (9.7, 14.8) | 12.7 (10.0, 15.4) | 0.2 |
| K Crude       | 0.6 (0.4, 0.8)           | 0.3 (0.1, 0.5) | 0.4 (0.2, 0.7) | 0.2 (0.0, 0.4) | <0.05 |
| K Model 1$^3$ | 0.5 (0.2, 0.8)           | 0.3 (0.1, 0.5) | 0.4 (0.2, 0.6) | 0.2 (0.0, 0.5) | 0.2 |
| K Model 2$^4$ | 0.6 (0.3, 0.9)           | 0.3 (0.2, 0.5) | 0.4 (0.2, 0.7) | 0.2 (0.0, 0.5) | 0.1 |

---

$^1$ Analysis of covariance.  
$^2$ All values are expressed as least square mean (95% confidence interval) of serum vitamin level.  
$^3$ Adjusted for gender, age, body mass index, and total energy intake.  
$^4$ Additionally adjusted for estimated glomerular filtration rate, urine pH, smoking status, and drinking status based on Model 1.
dation to its more toxic metabolite retinoic acid. This hypothesis postulates that the shared role of xanthine oxidase can result in hyperuricemia and hypervitaminosis A toxicity when retinol or xanthine levels are increased due to increased production or decreased renal excretion of these factors (19).

Positive association between levels of SUA and vitamin B5 were found in the present study. No previous study has explored the association between serum vitamin B5 and SUA levels. Vitamin B5 is also known as pantothenic acid. It is a component of coenzyme A and steroid hormone synthesis (20). Compared to the normal SUA level, total cholesterol significantly increases with a high SUA level (21). Thus, vitamin B5 may affect the SUA level.

Vitamins C and D2 were found to be inversely related to SUA concentrations and dependent on dietary and other risk factors, including age, sex, BMI, and total energy intake. These results suggest that there may be some associations between covariates and serum vitamins and/or SUA levels. For example, known lifestyle predictors of SUA level concentrations include dietary factors, such as meat, seafood, dairy intake, and dietary patterns (22). Serum vitamin concentrations are associated with dietary factors. Thus, the associations between vitamins C and D2 and SUA may be confounded.

However, as suggested by prior meta-analysis, patients with both vitamin D insufficiency and deficiency have a significantly higher level of SUA compared to individuals with normal vitamin D levels (14). In the present study, vitamin D insufficiency was defined as vitamin D levels of 20–30 ng/mL. The average vitamin D level was 21.13 ng/mL and the highest serum vitamin D level was only 32.85 ng/mL. Thus, participants with low serum level of vitamin D may have had insignificant results. In addition, a study among Chinese Han postmenopausal women suggested that vitamin D insufficiency is significantly associated with elevated SUA levels. Association between vitamin D insufficiency and elevated uric acid was not significant among premenopausal women (23). Therefore, the insignificant association between vitamin D and SUA levels may contribute to the unbalanced gender ratio and the fact that most participants were younger.

To the best of our knowledge, this is the first study to analyze the associations between various serum vitamins and SUA levels among Northeast Chinese adults. It provides scientific data necessary for controlling the development of hyperuricemia. However, several study limitations need to be noted. First, due to its cross-sectional design, the present study was unable to ascertain the temporality of associations. Thus, confirming the association with prospective longitudinal data (e.g., relationship between serum vitamin levels and SUA) is necessary. Second, residual confounding by unmeasured or poorly measured covariates cannot be ruled out. Third, a small overall sample size limited study precision for the estimations of biomarkers. Fourth, the study lacks the data on dietary intake, an important component of nutrient status assessment. Therefore, the association between dietary vitamin intake and SUA levels was not analyzed. Fifth, Shenyang in northeastern China is at latitude 41 degrees north, it seems that there is little sunshine. Our results showed that serum vitamin D had been detected, and it is important to explore the association between dietary content and serum vitamin concentration. However, in this study, the association between dietary intake of vitamin D and serum vitamin D concentration was not investigated because of lack of nutrition data. Moreover, it cannot be determined that the vitamin concentration in the blood reflects the nutritional status of vitamin in the living body, such as vitamin A. However, we did not test the vitamin concentration of other tissue.

In conclusion, SUA are significantly associated with serum vitamins A, B9 and B5 levels. Considering the limitations of this meta-analysis, additional large prospective studies and randomized controlled trials adjusted for more dietary factors and other confounding factors are warranted to verify these findings.

**Authorship**

The authors’ responsibilities were as follows: Y.L., Y.X., Q.W., Q.C., and Y.Z. conceptualized and designed the study; Y.L., Y.X., and Q.W., analyzed and interpreted the data; Y.L., Y.X., and Q.W., wrote the initial manuscript; Y.L., Y.X., Q.W., Q.C., and Y.Z. reviewed the manuscript and approved the final manuscript.

**Disclosure of state of COI**

No conflicts of interest to be declared.

**Acknowledgments**

The authors thank the Department of Clinical Epidemiology in Shengjing Hospital Medical University of China. We thank all participants were included in this study. We thank International Science Editing (http://www.internationalscienceediting.com) for editing this manuscript.

**Financial support**

This work was supported by the National Key R&D Program of China (No. 2017YFC0907405).

**Supporting information**

Supplemental online material is available on J-STAGE.

**REFERENCES**

1) Lim DH, Lee Y, Park GM, Choi SW, Kim YG, Lee SW, Kim YH, Yung DH, Kang JW, Lim TH, Kim HK, Choe J, Hong S, Kim YG, Lee CK, Yoo B. 2019. Serum uric acid level and subclinical coronary atherosclerosis in asymptomatic individuals: An observational cohort study. Atherosclerosis 288: 112–117.

2) Xiang S, Zhang X, Xie X, Wang J, Zhou Q, Chen Z, Wang Y, Liu G, Han F, Chen J. 2019. High serum uric acid level is a mortality risk factor in peritoneal dialysis patients: a retrospective cohort study. Nutr Metab (Lond)
Feig DI, Kang DH, Johnson RJ. 2008. Uric acid and cardiovascular disease. *Rheumatology (Oxford)* 49: 1529–1538.

Singh G, Lingala B, Mithal A. 2011. Association between vitamin D insufficiency and cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. *Lancet* 379: 2050–2062.

Yu S, Yang H, Guo X, Zhang X, Zhou Y, Ou Q, Zheng L, Sun Y. 2016. Prevalence of hyperuricemia and its correlates in rural Northeast Chinese population: from lifestyle risk factors to metabolic comorbidities. *Clin Rheumatol* 35: 1207–1215.

Li DY, Yin WJ, Yi YH, Zhang BK, Zhao J, Zhu CN, Ma RR, Zhou LY, Xie YL, Wang JL, Zuo SR, Liu K, Hu C, Zhou G, Zuo XC. 2019. Development and validation of a more accurate estimating equation for glomerular filtration rate in a Chinese population. *Kidney Int* 95: 636–646.

Choi WJ, Ford ES, Curhan G, Rankin JL, Choi HK. 2012. Independent association of serum retinol and beta-carotene levels with hyperuricemia: A national population study. *Arthritis Care Res* 64: 389–396.

National Institute of Diabetes and Digestive and Kidney Diseases. 2012. Vitamin B. In: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury.

Yang WX, Ma Y, Hou YL, Wang YB, You CG. 2019. Prevalence of hyperuricemia and its correlation with serum lipids and blood glucose in physical examination population in 2015-2018: a retrospective study. *Clin Lab* 65.

Choi HK. 2010. A prescription for lifestyle change in patients with hyperuricemia and gout. *Curr Opin Rheumatol* 22: 165–172.

Peng H, Li H, Li C, Chao X, Zhang Q, Zhang Y. 2013. Association between vitamin D insufficiency and elevated serum uric acid among middle-aged and elderly Chinese Han women. *PLoS One* 8: e61159.