

Folate food source, usual intake, and folate status in Korean adults

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BACKGROUND/OBJECTIVES: The purposes of the study were to investigate folate intakes and plasma folate concentrations as well as estimate folate status in Korean healthy adults.

SUBJECTS/METHODS: A total of 254 healthy 19- to 64-year-old adults (68 men and 186 women) living in Seoul metropolitan area, Gumi, and Kwangju, Korea participated. Three consecutive 24-hour dietary recalls, information on folate supplementation, and fasting blood samples were collected from the subjects.

RESULTS: The mean dietary folate intakes were 587.4 and 499.2 µg dietary folate equivalent (DFE)/day for men and women, respectively. The median dietary intakes of men and women were 566.6 and 474.6 µg DFE/day, respectively. Forty subjects (16.7% of total) less total folate than the estimated average requirement (EAR). Folate intakes of 23.3% of men and 34.8% of women aged 19-29 years did not meet the EAR for folate. Major food sources consumed for dietary folate were baechukimchi (Chinese cabbage kimchi), rice, spinach, eggs, and laver, which provided 44% of dietary folate intake for the subjects. Plasma folate concentrations were 23.4 nmol/L for men and 28.3 nmol/L for women, and this level was significantly lower in men than in women. Approximately 13% of men and 3% of women were folate-deficient, and the percentages of subjects showing folate concentrations lower than 10 nmol/L were 27.9% of men and 6.4% of women.

CONCLUSIONS: Folate intakes of Korean adults in this study were generally adequate. However, one-third of young adults had inadequate folate intakes.

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INTRODUCTION

Adequate folate intake is important to maintain one-carbon transfer reactions, including synthesis of nucleic acids and amino acid metabolism. Resynthesis of methionine from homocysteine is one of the most folate-dependent reactions [1]. Inadequate dietary intake is a major factor associated with folate deficiency [2]. The primary sign of folate deficiency is megaloblastic anemia, and folate deficiency can promote elevation of the blood concentration of homocysteine, which is related with cardiovascular disease. Low folate intakes are also associated with the development of certain types of cancer, including colorectal, prostate, and breast cancer [3-4]. Folate plays a vital role in mechanisms that mediate the transfer of one-carbon moieties required for DNA synthesis, stability and integrity, and repair [5]. Folate is widely distributed in foods such as dark green leafy vegetables, fruits, nuts, liver, and yeast. Major folate-containing food sources for Koreans have been reported as kimchi, rice, eggs, laver, spinach, and strawberries [5,6].

The Dietary Reference Intakes for Koreans include recommendations based on data from controlled metabolic studies

in which blood folate concentrations were measured as well as data from population-based studies [7]. The use of an appropriate cutoff is essential to accurately assess folate status. A plasma (serum) folate level less than 6.8 nmol/L is commonly used a cutoff to assess folate status [1,7,8]. However, in 2005, the World Health Organization (WHO) Technical Consultation recommended a new cutoff for possible deficiency on the basis of rising plasma homocysteine levels as a metabolic indicator (plasma folate concentration < 10 nmol/L) [9,10]. Although the dietary folate intake status of Koreans has been recently reported, current population-based studies on the current folate status of Korean adults including biochemical index are limited. Prior studies conducted in Korea have reported the folate status of non-pregnant women of childbearing age [11], pregnant or lactating women [12-14], university students [5,15], and the elderly [16]. The latest study regarding the folate status of Korean healthy adults including men was reported in 2001, and 13% of Koreans indicated folate deficiency based on plasma folate concentration [17]. Currently, no study has reported the folate status of Korean adults using a metabolic indicator proposed by the WHO. Moreover, as sources of folate may have changed among younger generations in Korea, it is necessary

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to evaluate the current diet of adults using dietary intake and biomarkers in order to address public health interventions. Therefore, the aims of this study were to determine folate intakes and food sources in adults living in South Korea as well as assess folate status.

SUBJECTS AND METHODS

Participants

A total of 275 Korean adults aged 19-64 years were recruited by advertisement in a convenience sampling of universities, gyms, and welfare centers in the Seoul metropolitan area, Kwangju, and Gumi from 2009 to 2011. All procedures were approved by the Institutional Review Board of Duksung Women's University (No. 2011-04-0001). Written informed consent was obtained from all subjects. The participants were interviewed to collect information regarding age, previous and current illnesses, recent changes of appetite and food intake, and medications being taken by well-trained interviewers. Subjects with current diagnosed diseases such as diabetes, cancer, cardiovascular disease, and kidney disease, subjects taking medications affecting folate metabolism, subjects showing recent changes appetite and food intake, and subjects that did not finish their 3-day food recall were excluded; therefore, final subjects were 253 adults. Characteristics of the participants are given in Table 1.

Assessment of folate intakes

A 3-day recall method was used to record the dietary intakes of the subjects: 2 days during the week and 1 day on the weekend. Dietary intakes were converted by using the computerized dietary analysis program Can-pro 4.0 [18]. Subjects were asked whether or not they had taken any dietary supplements within the last 30 days prior to the interviews. Forty-three subjects (16.9% of total subjects) took supplements containing folic acid; therefore, folate intakes in this study were reported as dietary folate and total (dietary plus supplemental) folate. Due to differences in the bioavailability of food folate and folic acid, folate intake in this study was expressed as dietary folate equivalents (DFE) [19].

$$\mu\text{g DFE} = \mu\text{g of food folate} + (1.7 \times \mu\text{g of folic acid})$$

Folate intakes were compared with the estimated average requirements (EAR), which are set at 320 $\mu\text{g DFE/day}$ for men

and women aged 19-64 years [19]. The quantitative contributions of various foods to the subjects' daily dietary folate intakes were determined, as previously described [20]. The percentage of subjects' consumption of each major source was also reported.

Blood samples and plasma measurements

After overnight fasting, venous blood was collected from subjects for assessment of folate status. Immediately following blood drawing in an EDTA-containing vacutainer, blood was centrifuged for 10 minutes at 3,000 rpm at 5°C. The plasma samples were stored at -70°C until analysis. Plasma folate concentrations were estimated using a microbiological method using *Lactobacillus casei* (ATCC 7469) with a 96-well microplate reader, and each sample was analyzed in triplicate [21] and expressed as nmol/L. The interpretive criterion for plasma folate concentration was less than < 6.8 nmol/L for folate deficiency [9] and a cutoff < 10 nmol/L was also used to indicate folate deficiency as a metabolic indicator based on the plasma folate concentration below which total homocysteine becomes elevated [9,10,22].

Statistical analyses

The subjects were grouped into three age groups: 19-29 years, 30-49 years, and 50-64 years and also grouped by gender. Student's t-test was used to investigate the differences between men and women in general characteristics. Folate intakes were reported as means \pm standard deviations (SD) by age groups in male and female subjects. One-way ANOVA followed by Duncan's multiple range test was used to determine differences in intake and plasma concentrations of folate among age groups. Pearson's partial correlation coefficient was calculated to determine possible relationships among folate intakes and plasma folate level after controlling for age, gender, body mass index, and energy intake [16]. Statistically significant differences were considered at *P* values < 0.05. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Folate intake of the subjects

Table 2 lists folate intakes of Korean adults. Daily dietary folate intakes of men and women were 587.4 ± 244.6 and 499.2 ± 214.0 $\mu\text{g DFE}$, respectively. Dietary and total folate intakes of men were significantly higher than those of women, whereas no significant difference in folate intake density was observed. Forty subjects (16.7%) consumed total folate less than the EAR. Women aged 19-29 years had the lowest folate intakes compared to the intakes of other age groups, but there were no differences in folate intakes among age groups in men.

Major food sources of folate

The major food sources of folate consumed by the subjects are shown in Table 3. Baechukimchi (Chinese cabbage kimchi), polished rice, spinach, hen's eggs, and laver were the top five foods, which provided 44.36% of dietary folate intake. The top 30 foods provided 77.82% of dietary folate intake. Baechukimchi and polished rice contributed 22.68% and 6.31%, respectively, of dietary folate intake.

Table 1. General characteristics of study participants.

	Men (n = 68)	Women (n = 186)	Total (n = 254)
Age, yrs**	36.4 \pm 13.3	41.1 \pm 12.3	39.8 \pm 12.7
19-29 yrs (n (%))	30 (44.1)	46 (24.7)	76 (29.9)
30-49 yrs (n (%))	21 (30.9)	83 (44.7)	104 (40.9)
50-64 yrs (n (%))	17 (25.0)	57 (30.6)	74 (29.1)
Anthropometric measurement			
Height (cm)***	172.4 \pm 6.4	159.5 \pm 4.3	163.0 \pm 7.5
Weight (kg)***	69.9 \pm 9.0	56.9 \pm 7.5	60.4 \pm 9.8
BMI (kg/m ²)**	23.5 \pm 2.6	22.4 \pm 2.8	22.7 \pm 2.8

Values are means \pm SD and number of people (% of total).

* *P* < 0,05, ** *P* < 0,01, *** *P* < 0,001 by Student's t-test.

Table 2. Folate intakes of study participants by gender and age.

	Men				Women			
	19-29 yrs	30-49 yrs	50-64 yrs	Total	19-29 yrs	30-49 yrs	50-64 yrs	Total
Dietary folate intake ($\mu\text{g DFE/day}$) ^{**}	573.0 \pm 293.0	557.3 \pm 219.8	649.9 \pm 169.5	587.4 \pm 244.6	383.4 \pm 185.0 ^b	523.9 \pm 218.9 ^a	556.6 \pm 195.7 ^a	499.2 \pm 214.0
Dietary folate per energy intake ($\mu\text{g DFE}/1,000 \text{ kcal/day}$)	268.3 \pm 144.3	253.5 \pm 105.8	332.3 \pm 98.8	279.7 \pm 125.1	239.0 \pm 123.4 ^b	305.5 \pm 116.1 ^a	317.7 \pm 111.6 ^a	292.8 \pm 120.1
Total folate intake ¹⁾ ($\mu\text{g DFE/day}$) [*]	633.7 \pm 330.8	654.5 \pm 288.5	669.9 \pm 175.0	649.2 \pm 282.4	455.8 \pm 264.8 ^b	571.0 \pm 261.8 ^a	621.5 \pm 255.9 ^a	557.9 \pm 266.8
Using supplements with folate (n (%))	5 (16.7)	6 (28.6)	1 (5.9)	12 (17.6)	10 (21.7)	11 (13.3)	10 (17.5)	31 (16.7)
Not meeting the EAR with dietary folate (n (%))	7 (23.3)	3 (14.3)	0 (0)	10 (14.7)	19 (41.3)	11 (13.3)	5 (8.8)	35 (18.8)
Not meeting the EAR with total folate (n (%))	7 (23.3)	1 (4.8)	0 (0)	8 (11.8)	16 (34.8)	11 (13.3)	5 (8.8)	32 (17.2)

Values are means \pm SD and number of people (% of total).

The estimated average requirement (EAR) for folate is 320 μg dietary folate equivalent (DFE)/day for Korean adults. A significant difference was observed by gender.

* $P < 0.05$ and ** $P < 0.01$ by Student's t-test.

¹⁾ Dietary + supplemental folate.

^{ab} Means within a row followed by the same letter are not significantly different at $P < 0.05$ by Duncan's multiple-range test.

Table 3. Major food sources of dietary folate of study participants.

Rank	Description	% T ¹⁾	% C ²⁾	% F ³⁾
1	Kimchi, Baechukimchi (Chinese cabbage)	22.68	22.68	96.46
2	Polished rice	6.31	28.99	98.82
3	Spinach	5.99	34.98	50.79
4	Hen's eggs	5.52	40.50	89.76
5	Laver	3.86	44.36	78.74
6	Mandarin	3.72	48.08	58.66
7	Soybean sprout	2.97	51.05	47.24
8	Beer	2.42	53.47	12.99
9	Welsh onion	2.39	55.85	95.28
10	Sweet potato	1.89	57.74	22.83
11	Radish root	1.59	59.33	68.11
12	Black soybeans	1.52	60.85	38.19
13	Kimchi, gatkimchi (mustard leaves)	1.47	62.33	6.69
14	Chinese cabbage	1.39	63.72	18.11
15	Strawberry	1.35	65.07	6.69
16	Cow's milk	1.23	66.30	45.67
17	Bracken	1.16	67.46	25.98
18	Dumpling	1.02	68.48	11.81
19	Doenjang (bean paste)	0.97	69.45	61.02
20	Cabbage	0.94	70.39	38.58
21	Lettuce	0.85	71.25	29.53
22	Young pumpkin	0.84	72.09	59.84
23	Garlic	0.83	72.92	98.43
24	Radish leaves	0.77	73.69	15.75
25	Soy sauce	0.75	74.43	97.64
26	Potato	0.73	75.16	61.02
27	Anchovy (<i>engraulis japonicus</i>)	0.73	75.88	31.50
28	Soybean milk	0.70	76.58	10.63
29	Onion	0.68	77.26	92.91
30	Green hot pepper	0.56	77.82	63.78

¹⁾ Percent of dietary intake of total subjects

²⁾ Cumulative percent of dietary intake

³⁾ Percent frequency of subjects consuming the food

Table 4. Plasma folate concentrations of study participants by gender and age.

	Men				Women			
	19-29 yrs	30-49 yrs	50-64 yrs	Total	19-29 yrs	30-49 yrs	50-64 yrs	Total
Plasma folate (nmol/L)*	21.2 \pm 19.1	23.3 \pm 13.6	27.5 \pm 15.3	23.4 \pm 16.6	23.6 \pm 14.1 ^b	28.3 \pm 14.5 ^{ab}	32.0 \pm 15.5 ^a	28.3 \pm 15.0
Subjects having plasma folate < 6.8 nmol/L (n (%))	7 (23.3)	1 (4.8)	1 (5.9)	9 (13.2)	4 (8.7)	2 (2.4)	0 (0)	6 (3.2)
Subjects having plasma folate < 10 nmol/L (n (%))	13 (43.3)	4 (19.0)	2 (11.8)	19 (27.9)	0 (0)	8 (9.6)	1 (1.8)	9 (4.8)

Values are means \pm SD and number of people (% of total). The significant difference was observed by gender.

* $P < 0.05$ by Student's t-test.

^{ab} Means within a row followed by the same letter are not significantly different at $P < 0.05$ by Duncan's multiple-range test.

Plasma folate concentration and folate status

Mean plasma folate concentrations were 23.4 \pm 16.6 nmol/L in men and 28.3 \pm 15.0 nmol/L in women, and a significantly higher plasma folate concentration was observed in women than in men ($P < 0.05$) (Table 4). The mean plasma folate concentration of women aged 19-29 years was significantly lower than that of women aged 50-64 years. Approximately 13.2% of men and 3.2% of women showed folate concentrations lower than 6.8 nmol/L, indicating folate deficiency in adults [9]. Percentages of subjects with a plasma folate concentration less than 10 nmol/L were 27.9% for men and 4.8% for women. Plasma folate concentration showed positive correlations with dietary ($r = 0.17659$, $P = 0.0048$) and total folate intakes ($r = 0.32866$, $P < 0.0001$).

DISCUSSION

The importance of folate in human health is well recognized, and inadequate folate status is associated with high risks of birth defects, anemia, and cardiovascular disease. Therefore, studying the current intake and status of folate population is essential for implementation of an effective public health program. For healthy adult men and women in Korea, an EAR of 320 $\mu\text{g DFE/day}$ was proposed based on the results of a study conducted by O'Keefe *et al.* [23] in which a specified quantity of dietary folate was inadequate for maintaining normal folate status in half of all subjects. The recommended nutrient intake (RNI) for folate is 400 $\mu\text{g DFE/day}$ for adults [7].

The mean dietary folate intakes of men and women in the current study were 587.4 and 499.2 $\mu\text{g DFE/day}$, respectively, which are much higher than the RNI and folate intake of Korean college students reported in 2013 (456 for men, 347 $\mu\text{g DFE/day}$ for women) [15]. Compared to the intakes of other populations, the folate intake in this study was found to be higher than

those of Chinese adults (291.4 µg/day) [24] and British adults (287 for men, 228 µg DFE/day for women) [25] and similar to the intake of American adults (650 for men, 490 µg DFE/day for women) [26]. Small proportions of participants in this study had dietary folate intakes below the EAR (14.7% of men, 18.8% of women). Thus, folate intake of the subjects was generally adequate. However, certain age groups may be at risk of insufficient folate intakes. In this study, total folate intakes of 34.8% for women and 23.3% for men aged 19 to 29 years did not meet the EAR.

Folate that occurs naturally in the diet is concentrated in selected foods, including green leafy vegetables, fruits, beans, seaweeds, and eggs. Strawberries, oranges, kiwis, and Oriental melon also contain significant amounts of folate [7]. In addition to food folate, folic acid is fortified in ready-to-eat breakfast cereals, infant formulas, meal replacements, and nutritional bars. The top 10 dietary sources of folate in the current study were baechukimchi (Chinese cabbage kimchi), polished rice, spinach, eggs, laver, mandarin, soybean sprout, beer, welsh onion, and sweet potato, which provided 57.74% of dietary folate intake. As the top food, baechukimchi provided 22.68% of dietary folate intake. Vegetables and fruits were principal folate-contributing foods, and they are typical of the Korean diet. In Western countries such as the UK and US, cereals and cereal products are the largest contributors of folate, and large amounts of folate intake come from ready-to-eat breakfast cereals and bread (most of which are fortified with folic acid) [25]. However, except for polished rice, no cereal or cereal product was included in the top 30 foods in this study.

The mean plasma folate levels of men and women were 23.4 nmol/L and 28.3 nmol/L, respectively, which are in line with the levels of Korean college students [15]. However, the prevalence of folate deficiency (6.5 nmol/L) in this study was higher than the prevalence of folate deficiency in Korean college students (3.8% in men, 0% in women) [15]. Approximately 12% of subjects had plasma folate concentrations below the WHO cutoff, indicating folate deficiency (10 nmol/L). Insufficient folate intake is a major cause of folate deficiency, although folate deficiency can also occur in other situations [27]. As previously stated, folate intake of Korean adults in this study was much higher than those of other populations. Retention of folate in foods after cooking is variable and highly dependent on type and method of food preparation [28], and it has been reported that food folate is reduced by 50% to 80% with food processing and preparation [29]. In this study, dietary intakes were analyzed based on a food composition table based on nutrient contents of foods generally in the raw state. In Western countries, major food sources such as ready-to-eat cereals, breads, and folate-fortified foods are not affected by cooking method.

The WHO recommended a new cutoff < 10 nmol/L of plasma folate for possible folate deficiency as a metabolic indicator based on the plasma folate concentration below which total homocysteine become elevated [9,10]. It is known that homocysteine in the blood promotes cardiovascular problems due to its negative effects on the cardiovascular endothelium and smooth muscle cells [30]. In the current study, folate deficiency was higher in men than in women, and over one-fourth of men had a plasma folate level less than the metabolic

indicator. Winkels *et al.* [31] reported that the erythrocyte folate level in response to folic acid supplementation in males decreased compared to that in females after a daily dose of 800 µg of folic acid in a 3-year trial, and the gender difference might be due to the higher average lean body mass size of men. van der Griend *et al.* [32] reported that plasma folate levels were significantly lower in men than in women after an 8-week trial with 500 µg/day of folic acid. In this study, folate intake of men was significantly higher than that of women, whereas plasma folate concentration was significantly lower in men than in women, which has also been reported by other studies [16,33,34]. Therefore, men may require more folate intake to improve folate status and to reduce risk of cardiovascular disease.

Several limitations may restrict the generalizability of the results in this study. First, plasma folate was used to assess folate status. For population surveys, plasma folate measurement is suitable to assess general folate status [35]. However, plasma (serum) folate level is subject to diurnal changes caused by recent food intake and thus cannot be used to distinguish between a transitory decrease in folate intake and chronic deficiency states [9]. On the other hand, red blood cell folate reflects long-term body folate status in that it indicates the average folate content of long-lived red blood cells [9]. Total homocysteine level in plasma is used as a functional test of folate deficiency. Future studies should confirm findings based on red blood cell folate or total homocysteine. Second, lifestyle factors that affect folate status were not assessed in this study. Cigarette smoking, excessive alcohol use, and oral contraceptive agents may cause lowering of plasma folate levels [2,7]. In addition, the limited numbers and random selection of subjects in this study might limit the representability of Korean healthy adults. Nonetheless, this study provides practicable information to assess the folate status of Korean adults.

In conclusion, folate intakes of Korean adults in this study were generally adequate, whereas one-third of young adults were characterized by inadequate folate intake. The prevalence rates of folate deficiency were 13% in men and 3% in women. In this study, men were shown to be at higher risk of inadequate plasma folate levels, although folate intake was higher in men than in women. Health policies in the future should focus on increasing the supply and education related to a folate-rich diet for Korean men as well as young women. Future research is needed to assess folate status via other biochemical indices, including red blood cell folate or plasma total homocysteine, for more feasible assessment of folate status in Koreans.

CONFLICT OF INTEREST

The authors declare no potential conflicts of interests.

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