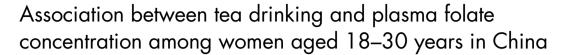


MS Public Health Nutrition



Xiaoqian Jia^{1,2}, Mengyuan Ren^{1,2}, Yali Zhang^{1,2}, Rongwei Ye^{1,2}, Le Zhang^{1,2,*} and Zhiwen Li^{1,2,*}

¹Institute of Reproductive and Child Health/National Health Commission Key Laboratory of Reproductive Health, Peking University Health Science Center, Beijing 100191, China: ²Department of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Center, Beijing 100191, China

Submitted 19 June 2020: Final revision received 9 October 2020: Accepted 24 November 2020: First published online 15 December 2020

Abstract

Objective: Association was found between tea and neural tube defects. However, few studies investigated the relationship between tea consumption and blood folate levels. We aimed to investigate the association between tea consumption and plasma folate concentrations among women aged 18–30 years in different ethnicities of China.

Design: Data were obtained from a national cross-sectional study conducted from 2005 to 2006 of women aged 18–30 years in China. Socio-demographic characteristics and lifestyle were obtained from a questionnaire. Dietary folate intake was determined by 24-h dietary recall. Plasma folate concentrations were measured by a microbiological assay. Multiple linear regression model was used to calculate partial regression coefficients after adjusting for confounding factors.

Setting: Nine provinces or autonomous regions in China.

Participants: A total of 2932 women aged 18-30 years in China.

Results: After stratifying by ethnicity and tea type, tea consumption was significantly positively associated with plasma folate levels in Han women who drank unfermented tea weekly (β =0·067, and P=0·037) or daily (β =0·119, and P=0·031) and in Uighur women who drank fermented tea weekly (β =0·325, and P=0·028). For women who drank unfermented tea in Han ethnicity, weekly and daily tea drinkers had 6·77 % (95 % CI: 6·36 %, 7·21 %) and 7·13 % (95 % CI: 6·40 %, 7·96 %) increase in plasma folate concentration compared with no tea drinkers.

Conclusions: There is a suggestion of possible positive association between unfermented tea drinking in Han ethnicity and plasma folate concentrations, for Chinese women aged 18–30 years. The relationship between tea drinking in other ethnic groups and plasma folate still needs to be further explored.

Keywords Tea Plasma folate Dietary folate intake Women aged 18–30

Folate deficiency during the periconceptional period has been strongly confirmed as a risk factor for many adverse pregnancy outcomes, especially neural tube defects (NTD)^(1,2). Therefore, any factors affecting folate levels may be associated with NTD.

Tea is the most popular beverage worldwide. It is consumed by two-thirds of the world's population, and drinking tea has been considered a health-promoting habit since ancient times⁽³⁾. However, several studies have found that drinking tea was associated with an increased risk for NTD under the condition with no consideration of dietary folate intake. A case–control study conducted in northern China

showed that women who drank tea every day were over three times more likely to have an NTD-affected pregnancy compared with those who did not drink tea⁽⁴⁾, and another case–control study conducted in America found an increased risk of spina bifida associated with daily consumption of tea⁽⁵⁾. A hypothesised mechanism for this association was that tea intake may affect the absorption and metabolism of folate⁽⁶⁾. In addition, Yazdy *et al.* studied the relationship between tea consumption and spina bifida after adjusting for dietary folic acid (FA) intake after 1988, and they think there is a suggestion of a possible interaction between higher levels of FA intake and tea consumption.

*Corresponding author: Email zhangle@bjmu.edu.cn; lizw@bjmu.edu.cn © The Author(s), 2021. Published by Cambridge University Press on behalf of The Nutrition Society





However, the results of these interactions were not statistically significant (OR range contained 1·00), which may be due to the small sample size of each group after stratification⁽⁷⁾. Animal experiment shows that high levels of green tea catechins can decrease serum 5-methyltetrahydrofolate concentrations of rats⁽⁸⁾.

Previous epidemiological studies have investigated the association between tea consumption and blood folate levels, but results have been inconsistent. An open-label randomised crossover study revealed that consumption of green or black tea was associated with a low serum folate level for healthy volunteers⁽⁹⁾. A cross-sectional survey showed no association between tea drinking and plasma folate concentrations in pregnant Chinese women with high and low prevalence of NTD⁽¹⁰⁾. However, most studies did not take into account the effects of dietary folate intake, despite its being the most important factor for folate levels in the body other than FA supplement. Therefore, the aim of this study was to determine whether tea drinking was associated with plasma folate concentration in women aged 18-30 years in China after adjusting for confounding variables including dietary folate intake, FA supplement and BMI. Moreover, China is a multi-ethnic country, and different ethnic groups have its own tea drinking characteristics, especially tea types, so, we further analysed the relationship between tea drinking and plasma folate concentration after stratifying by ethnics and tea types.

Materials and methods

Study design and selection of participants

This study was based on a nationwide cross-sectional study designed to investigate the nutritional status of women aged 18-30 years in areas with different levels of economic development in China; this study was partly described elsewhere (11). It was conducted in nine provinces or autonomous regions in China, including Inner Mongolia, Gansu, Liaoning, Shandong, Sichuan, Guangdong, Xinjiang Uygur, Guangxi and Hubei; in each province, one city and one county were selected as project sites. The study was conducted during two periods (April to May 2005 and October 2005 to April 2006). One hundred women were planned to be recruited in each city or county during each period. The inclusion criteria were (1) 18-30 years of age, (2) not pregnant or breast-feeding, (3) living in the area for more than 1 year and (4) free from hypertension, diabetes, cancers, and heart, liver, renal and gastrointestinal diseases, as well as other serious diseases. A total of 3660 women were recruited from 2005 to 2006, of whom 3269 women were eligible, 203 (5.55 %) were excluded because of age and 188 (5.14%) were excluded because of the diseases mentioned above.

We conducted the present study using data collected in the study described above. Of 3269 eligible women, we excluded 174 (5.32%) with missing data on plasma

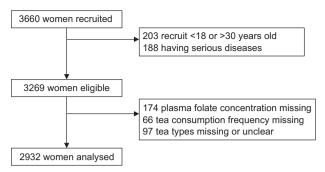


Fig. 1 The flow chart of participants in this study

folate concentration, 66 (2.02%) with missing data on tea consumption frequency and 97 (2.97%) with missing or unclear information on tea types. After these exclusions, 2932 targeted participants (89.69% of eligible women) were included in the final analysis. The flow chart of participants in this study was presented in Fig. 1.

Measurements and definitions of major variables

At the community health centre, a trained interviewer administered a structured questionnaire to subjects to collect data on socio-demographic and personal characteristics, including age, ethnicity, educational level, current cigarette and alcohol use, use of oral contraception, and use of FA supplements or multivitamins containing FA. FA supplement was defined as a self-report of having taken FA supplements or multivitamins containing FA in the past 3 months. Dietary data were collected using 24-h recall through face-to-face interview by trained nurses for one time, with two-dimensional drawings of bowls and plates to estimate portion sizes. Dietary folate intake levels were calculated based on Chinese Food Composition⁽¹²⁾. Dietary folate concentrations were adjusted by energy intake to minimise the influence of dietary false reporting⁽¹³⁾, calculating through 1000*dietary folate concentrations (µg)/ energy intake (kcal). Dietary folate was divided into three groups according to the 25th and 75th percentiles of its natural logarithm (low: 3.07-4.46, medium: 4.47-5.08 and high: 5.09-7.43). It is worth noting that there was no promotion and use of folate-fortified foods in China. Therefore, the folate intake of the study population was mainly derived from dietary folate intake.

Body weight in light clothing and height without shoes were measured to the nearest $0.1 \, \mathrm{kg}$ and $0.1 \, \mathrm{cm}$ with a beam weighing scale and a height scale, respectively. BMI was calculated as weight (kg)/height (m)². Underweight, normal weight, overweight and obese were defined according to the standards recommended by the Working Group on Obesity in China⁽¹⁴⁾ (underweight: BMI < $18.5 \, \mathrm{kg/m^2}$; normal weight: BMI = $18.5-23.9 \, \mathrm{kg/m^2}$; overweight: BMI = $24.0-27.9 \, \mathrm{kg/m^2}$ and obese: BMI > $28.0 \, \mathrm{kg/m^2}$).



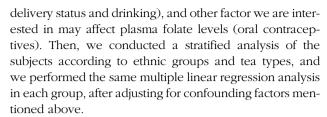
Subjects were asked 'how many days have you drunk tea each week over the past three months?' If the answer was one to seven (not zero), they were further asked what type of tea they usually drank. We defined 0 d a week as no tea consumption, while 1–7 d(s)/week as tea consumption. The type of tea was divided into two categories according to different production processes: fully fermented tea (black tea and compressed tea) and unfermented tea (green tea and scented tea)⁽¹⁵⁾. Smoking was defined as smoking at least one cigarette per day for six consecutive or cumulatively months and above. And drinking alcoholic beverage was defined as drinking alcohol more than once a month in the last year.

Overnight fasting blood (9 ml) was collected from each subject by venepuncture by a qualified nurse. Blood samples were drawn into K3EDTA-containing Vacutainer tubes (Becton Dickinson) and centrifuged within 1 h of collection. Plasma and erythrocytes were separated and frozen at -20 °C. All specimens were transported on dry ice to the central laboratory of the Institute of Reproductive and Child Health, Peking University, and stored at -70 °C before nutritional analyses. Plasma folate concentrations were determined by a microbiological assay⁽¹⁶⁾. The intraand inter-assay coefficients of variation were less than 9 % across the full range of folate concentrations.

Statistical analysis

Sample size was determined based on a cross-sectional study conducted in China, which geometric mean concentrations of plasma folate acid for women were $23\cdot0\pm11\cdot8$ and $18\cdot2\pm9\cdot3$ nmol/l in spring and fall, respectively⁽¹⁷⁾. Then, statistical power and the two-sided significance level were set to be 90 % and 0·05. For the original research, the minimum sample size should be 208 women. However, for this research, we calculated that under the condition of a sample size of 2932, the test power was 1·00, which can meet the research requirement.

The Little's MCAR test was done to test whether the missingness was completely at random. The basic characteristics of participants in the different study groups were compared using Student's t test for quantitative variables, the χ^2 test for non-ordered categorical variables and the Kruskal-Wallis test for ordered categorical variables. The distributions of dietary folate intake and plasma folate concentrations adjusted by energy were positively skewed, so geometric means and interquartile range were used to describe their distributions, and values were logtransformed before further analysis, including t tests. We used multiple linear regression to evaluate the partial correlation coefficients with 95 % CI after adjusting for confounding factors. These factors include mentioned in previous studies (age, education, delivery status, FA supplement, smoking, BMI and concentration of dietary folate adjusted by energy)(10,11,13), imbalanced between tea consumption and no tea consumption group (ethnicity,



SPSS for Windows software (ver.20.0; SPSS, Inc.) was used for statistical analyses, and two-sided P < 0.05 was considered significant.

Results

Basic characteristics of targeted participants are shown in Table 1. Approximately 46.1% (1353) of these women reported that they drank tea in the past 3 months; these women were more likely to be Mongolian or Uighur (23.2% or 16.0% v. 0.4% or 2.1%), educated through high school or higher (60.4% v. 45.7%), occupation type was others or unemployed (57.5% or 11.2% v. 35.5% or 9.4%), primiparous (48.1% v. 38.9%), drinking alcoholic beverage (11.6% v. 3.9%) and overweight or obese (16.0% or 3.5% v. 11.5% or 2.0%) compared with the no tea drinking group. Women who consumed tea had significantly lower geometric mean dietary folate adjusted by energy (112·86 μg/1000 kcal) and plasma folate levels (12.92 nmol/l) compared to women who did not consume tea (127·24 µg/1000 kcal and 16·77 nmol/l, respectively). However, there were no significant differences between the two groups in oral contraceptive use, FA supplement use and smoking.

The Little's MCAR test was used in SPSS for the missing data, when quantitative variable was log-transformed plasma folate levels, and categorical variables were education, occupation, oral contraceptives, delivery status, FA supplement, smoking and BMI. $\chi^2 = 0.103$, and P = 0.749. So the missingness was completely at random.

Table 2 shows the relationship between log-transformed plasma folate concentrations and concerned factors. Ethnicity was a significant predictor of log-transformed plasma folate levels. When the Han ethnic group was used as the reference group, Mongolian and Uygur women had lower folate levels (β =-0.606 and -0.614), and Zhuang women had higher folate levels (β =0.342). High dietary folate intake was associated with increased log-transformed plasma folate levels (β =0.154, P<0.001), and high BMI was inversely correlated with log-transformed plasma folate. Tea drinking frequency had no statistical association with log-transformed plasma folate levels after adjusting for confounding variables (weekly and daily tea drinking, P=0.063 and 0.204, respectively).

Further analyses were conducted to examine the relationship between tea drinking frequency and log-transformed plasma folate concentrations stratified by





Table 1 Characteristics of Chinese women aged 18 to 30 years in the study

	All participants (n 2932)		Tea consumption (n 1353)		No tea consumption (n 1579)		
Characteristics	n	%	n	%	n	%	Р
Age (years) Mean	25.79		25.57		25.97		0.002*
SD	3.47		3.59		3⋅35		
Ethnicity	0010	CO 7	770	F7 4	1010	70.5	.0.001+
Han ethnic group Mongolian	2013 321	68∙7 10∙9	773 314	57⋅1 23⋅2	1240 7	78⋅5 0⋅4	< 0.001†
Uighur	249	8.5	216	16.0	33	2.1	
Zhuang ethnic group	349	11.9	50	3.7	299	18.9	
Education	0.0			٠.	_00		
Junior high school or lower	1385	47.2	531	39.2	854	54.1	< 0.001†
High school and secondary school	803	27.4	398	29.4	405	25.6	
College or higher	736	25.1	419	31.0	317	20.1	
Missing data	8	0.3	5	0.4	3	0.2	
Occupation	000	04.0	66.4	04.0	0.40	44.0	0.0041
Farmers	932	31.8	284	21.0	648	41.0	< 0.001†
Workers	340	11·6	126	9.3 57.5	214	13·6	
Others Unemployed	1339 301	45⋅7 10⋅3	778 152	57⋅5 11⋅2	561 149	35⋅5 9⋅4	
Missing data	20	0.7	132	1.0	7	0.5	
Oral contraceptives	20	0.7	10	1.0	,	0.0	
No	2750	93.8	1245	92.0	1505	95.3	0.102†
Yes	55	1.9	31	2.3	24	1.5	0 .021
Missing data	127	4.3	77	5.7	50	3.2	
Delivery status							
None	1265	43.1	651	48⋅1	614	38.9	< 0.001†
Yes	1479	50.4	590	43.6	889	56.3	
Missing data	188	6⋅4	112	8.3	76	4.8	
FA supplement							
No	2700	92.1	1235	91.3	1465	92.8	0.468†
Yes Missing data	218	7·4	67 51	5·0	70	4.4	
Missing data Smoking	95	0.5	51	3.7	44	2.8	
No	2851	97.2	1302	96.2	1549	98.1	0.060†
Yes	49	1.7	29	2.1	20	1.3	0.0001
Missing data	32	1.1	22	1.7	10	0.6	
Drinking alcoholic beverage							
No	2714	92.6	1196	88.4	1518	96.1	< 0.001†
Yes	218	7.4	157	11.6	61	3.9	
BMI							
Underweight	428	14.6	177	13.1	251	15∙9	< 0.001†
Normal weight	2018	68.8	904	66.8	1114	70.6	
Overweight	398	13.6	217	16.0	181	11.5	
Obese Mississedate	80	2.7	48	3.5	32	2.0	
Missing data	8	0.3	7	0.5	1	<0⋅1	< 0.001§
Concentration of dietary folate (μg) Mean	196 5	2 +	179.0	2+	10/ 1/	0 +	< 0.0018
Interquartile range	186·52‡		178·03‡ 124·87–		194·12‡ 137·13–		
interquartie range	131⋅69– 262⋅64		252.44		271·42		
Concentration of dietary folate adjusted by energy (µg/1000 kcal)	202	. 57	202		271		< 0.001
Mean	120	39‡	112	·86‡	127-24	4‡	
Interquartile range	86.73-			151.48		169.02	
Plasma folate (nmol/l)							< 0.001
Mean	14-8	87‡	12.	92‡		77‡	
Interquartile range	9.6	1–22.98	8.3	6–19-26	11.04-	-25.05	

No tea consumption group: 0 d/week; tea consumption group: 1-7 d/week.

‡Geometric mean (interquartile range).

§Mann–Whitney test.

IlStudent's t test was performed after computing natural logarithm of folate levels.



^{*}Student's t test.

 $[\]dagger \chi^2$ test.



Table 2 Multiple linear regression model on plasma folate concentration and related factors in Chinese women aged 18-30 years*,†,‡

				95 % CI		
Variables	n	β	P	Lower bound	Upper bound	
Age	2627	0.010	0.015	0.002	0.017	
Ethnicity						
Han ethnic group	1831	Ref	Ref	Ref	Ref	
Mongolian	257	-0.606	< 0.001	-0.705	-0.507	
Uighur	205	-0.614	< 0.001	-0.709	-0.518	
Zhuang ethnic group	334	0.342	< 0.001	0.276	0.408	
Education						
Junior high school or lower	1277	Ref	Ref	Ref	Ref	
High and secondary school	715	0.016	0.571	-0.040	0.072	
College and higher	635	0.042	0.213	-0.024	0.109	
Occupation						
Farmers	880	Ref	Ref	Ref	Ref	
Workers	320	-0.287	< 0.001	-0.360	-0.213	
Others	1178	–0.091	0.004	-0.152	-0.029	
Unemployed	249	-0.026	0.507	-0.104	0.051	
Oral contraceptives						
No	2575	Ref	Ref	Ref	Ref	
Yes	52	–0⋅157	0.036	-0.304	-0.010	
Delivery status						
None	1202	Ref	Ref	Ref	Ref	
Yes	1425	0.070	0.024	0.009	0.130	
FA supplement						
No	2501	Ref	Ref	Ref	Ref	
Yes	126	0.120	0.015	0.023	0.217	
Smoking						
No	2587	Ref	Ref	Ref	Ref	
Yes	40	–0⋅143	0.091	-0.308	0.023	
Drinking alcoholic beverage						
No	2454	Ref	Ref	Ref	Ref	
Yes	173	0.060	0.164	-0.024	0.144	
BMI						
Underweight	385	0.034	0.269	-0.026	0.094	
Normal weight	1812	Ref	Ref	Ref	Ref	
Overweight	357	-0.139	< 0.001	-0.200	-0.078	
Obese	73	–0⋅187	0.003	–0⋅313	-0.062	
Natural logarithm of dietary folate adjusted by energy						
Low	651	Ref	Ref	Ref	Ref	
Medium	1314	0.038	0.139	-0.013	0.089	
High	662	0.154	< 0.001	0.094	0.214	
Tea consumption§						
None	1459	Ref	Ref	Ref	Ref	
Weekly	638	0.049	0.063	-0.003	0.100	
Daily	530	0.051	0.204	-0.028	0.130	



[†]All of the variables in the table were included in the regression model.

ethnicity and tea types (Table 3). The results showed that in women of Han ethnicity, consuming unfermented tea weekly (β =0·067, P=0·037) or daily (β =0·119, P=0·031) was significantly associated with a higher log-transformed plasma folate level after adjusting for confounding variables. We further transformed β of the unfermented tea drinking group in Han ethnicity (the geometric mean of plasma folate concentration for those who did not drink tea in Han ethnicity was 15·79 nmol/l), and the results showed that when compared with no tea drinkers, weekly tea drinkers and daily tea drinkers had 6·77% (95% CI: 6·36%, 7·21%) and 7·13% (95% CI:6·40%, 7·96%) increase in plasma folate concentration, as shown in Supplemental Table S1.

In women of Uighur ethnicity, drinking fully fermented tea weekly was also positively associated with elevated plasma folate levels. However, no statistically significant correlation was found in other groups in this study.

Discussion

In this cross-sectional study, we examined the association between tea drinking and plasma folate concentrations among women aged 18–30 years in China. A total of 2932 women from four ethnic groups (Han and three national minorities) were included in this study. When we stratified by ethnicity and tea type, we found that tea

 $[\]sharp \beta$ values are per unit increase in log-transformed plasma folate levels.

[§]None = 0 d/week; Weekly: 1-6 d/week; Daily: 7 d/week.



Table 3 Multiple linear regression model on plasma folate concentration and tea consumption in Chinese women aged 18-30 years stratified by ethnicity and types of tea*,†

Variables		Fully fermented tea‡					Unfermented tea§					
	n	β	P	95 % CI lower bound	95 % CI upper bound	n	β	P	95 % CI lower bound	95 % CI upper bound		
Han												
None	1141	Ref	Ref	Ref	Ref		Ref	Ref	Ref	Ref		
Weekly	81	0.009	0.893	-0 ⋅121	0.139	473	0.067	0.037	0.004	0.129		
Daily	19	-0.257	0.058	-0.523	0.009	117	0.119	0.031	0.011	0.228		
Mongolian												
None	6	Ref	Ref	Ref	Ref		Ref	Ref	Ref	Ref		
Weekly	16	0.136	0.475	-0.239	0.511	3	-0.269	0.499	–1 ⋅116	0.578		
Daily	216	0.103	0.536	-0.224	0.431	16	0.223	0.291	-0 ⋅219	0.664		
Uighur												
None	26	Ref	Ref	Ref	Ref		Ref	Ref	Ref	Ref		
Weekly	17	0.325	0.028	0.035	0.616	1	_	_	_	_		
Daily	158	0.156	0.119	-0.041	0.353	3	0.029	0.937	-0.730	0.788		
Zhuang												
None	286	Ref	Ref	Ref	Ref		Ref	Ref	Ref	Ref		
Weekly	2	-0.156	0.598	-0.739	0.427	45	-0.017	0.815	-0 ⋅159	0.125		
Daily	0	_	_	_	_	1	0.375	0.367	-0.442	1.191		

^{*}Adjusted for age (continuous), education, occupation, oral contraceptives, delivery status, FA supplement, smoking, alcoholic beverage drinking, BMI and dietary folate intake adjusted by energy.

consumption was positively correlated with plasma folate concentrations in Han women who drank unfermented tea weekly or daily and in Uighur women who drank fully fermented tea weekly. And for women who drank unfermented tea in Han ethnicity, weekly and daily tea drinkers had 6.77 % (95 % CI: 6.36 %, 7.21 %) and 7.13 % (95 % CI: 6.40 %, 7.96 %) increase in plasma folate concentration compared with no tea drinkers. This is a suggestion of possible positive association between tea drinking and plasma folate concentrations.

Tea is second only to water as the most commonly consumed beverage (3), and regular tea consumption has been reported to have beneficial health, including cancer prevention^(18,19), cardiovascular benefits^(20,21) and neuronal disease prevention⁽²²⁾. This study revealed that 46·1% (1353/2932) of Chinese women aged 18-30 years drank tea at least once a week in the 3 months prior to the survey. This was higher than the 21.3% of Chinese women aged 30-79 years who consumed tea weekly as reported by Li X⁽²³⁾. This difference may be due to inclusion in our study of minorities with high tea consumption rates, such as Mongolian and Uighur women. Our results also showed that the dietary intake of folate adjusted by energy in this population (geometric mean = $120.39 \,\mu\text{g}/1000 \,\text{kcal}$ (interquartile range: 86·73–161·81)) was higher than that of pregnant women in Japan (median = $110 \,\mu g/1000 \,\mathrm{kcal}$ (interquartile range: 91-139)) and that the plasma folate concentration (geometric mean = 14.87 nmol/l (interquartile range: 9.61-22.98)) was higher than that of Japanese women (median = 11.2 nmol/l (95% CI: 8.6, 19.5))(11) but lower than that of women of childbearing age in the USA before cereal grain was fortified with 140 mg/100 g of FA during 1988-1994 (median = 15.3)nmol/l (95% CI: 14·3, 16·8))⁽²⁴⁾.

Only a few studies have explored the relationship between tea consumption and folate levels. Alemdaroglu et al. (9) found that consumption of green or black tea was associated with a low serum folate level in healthy volunteers, and Shiraishi et al. (13) found that high consumption of green tea or oolong tea was associated with low serum folate levels during pregnancy. The probable mechanism for such a relationship is that catechins in tea are similar to folate in structure and competitively bind to dihydrofolate reductase, affecting folate metabolism⁽⁶⁾. These catechins include epigallocatechin 3-gallate (constituting about 59 % of total catechins), epigallocatechin, epicatechin-3-gallate and epicatechin⁽²⁵⁾. However, Augustin et al. (8) pointed out that normal tea consumption levels did not reduce plasma folate concentrations, and a 70-kg human would have to drink almost 100 cups of green tea infusion per day to decrease serum folate concentrations via this mechanism. Moreover, few studies have controlled dietary folate intake, as stated above, which is an important factor that is significantly associated with plasma folate levels⁽²⁶⁾.

No association was found between tea drinking frequency and plasma folate concentrations when we adjusted for BMI and dietary folate adjusted by energy. However, when we stratified our analysis by ethnicity and tea types, we found that Han women drinking unfermented tea and Uighur women drinking fully fermented tea had higher plasma folate levels after adjusting for dietary folate intake. This may be due to the relatively large amount of folate in tea. Chen et al. (27) found that, of the



[†]There were no or few objects in this group.

[‡]Fully fermented tea: including black tea and compressed tea.

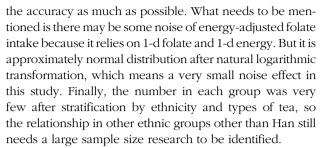
[§]Unfermented tea: including green tea and scented tea.



three major types of tea (green, black and oolong), green tea leaves possessed the highest total FA (TFA) content, with an average of 1.12 mg/100 g, and black tea leaves had a moderate amount of 0.73 mg/100 g. They also found that brewed green tea had the highest total FA content $(6.92 \,\mu\text{g}/100 \,\text{ml})$, followed by black tea $(5.16 \,\mu\text{g}/100 \,\text{ml})$. For these measurements, researchers used a standard procedure of adding boiling water to tea leaves at a ratio of 100:1 (w/w) and allowing an infusion time of 5 min⁽²⁸⁾. Meanwhile, the result of the China Kadoorie Biobank (CKB) survey revealed that Chinese women drank an average of 3.4 cups of tea each day⁽²³⁾. According to the standard cup volume of 300 ml, the daily intake of folate from drinking tea was about 70.6 µg and 52.6 µg from green tea and black tea, respectively. Similarly, Stagg et al. (28) considered that if five cups of tea were consumed daily, 6-13% of the RDA (400 µg) for folate would be obtained. Therefore, tea leaves and tea brews could be regarded as a good source of folate⁽²⁷⁾. Moreover, some cross-sectional population studies have found that a higher intake of tea was associated with lower total homocysteine (29), and they considered the folate in tea may contribute to lower total homocysteine⁽³⁰⁾. These studies provide some support for that drinking tea could increase plasma folate levels, but specific mechanisms remain to be identified.

Our result that different types of tea were correlated with plasma folate concentrations in different ethnicities may be due to differences in typical tea type consumption among ethnicities. The lack of relationship between tea consumption and plasma folate concentrations in Mongolian and Zhuang women may be that there were too few women who did not drink tea in Mongolian or drank tea in Zhuang nationality, respectively. Therefore, the correlation between tea consumption and plasma folate concentration in minorities requires further research to confirm. And the different relationship in different ethnicities may be due to differences in tea-making process, brewing methods and even different genetic information, especially methylenetetrahydrofolate reductase. Further research is needed to collect more comprehensive information, including methylenetetrahydrofolate reductase in different ethnicities, to investigate the exact influencing factors behind ethnic groups.

This study has several limitations. First, we used 'days/ week' to measure the frequency of tea consumption, which may not be accurate enough compared to 'cups/week' or 'ml/week'. And we did not collect information on the teamaking process, brewing methods, and so on, and these factors affect tea composition. Second, we did not measure erythrocyte folate concentrations in this study. Erythrocyte folate is stable in the human body for 3–4 months and would provide a better summary of folate status (31,32). Then, we used a 24-h recall method to collect dietary intake from the women, but this method was relied on personal memories and there may be exposure misclassification. However, we used two-dimensional drawings of bowls and plates to estimate portion sizes, which may improve



Our study also has several strengths. First, we controlled for the level of dietary folate intake, which strengthened our results. Most existing studies have not made this adjustment. Additionally, this study included populations in different areas of China, and diverse ethnicities and tea types were taken into account. This makes our result more comprehensive than most.

Conclusions

In conclusion, after stratifying by ethnic group and tea type, we found that Han women drinking unfermented tea and Uighur women drinking fully fermented tea had higher plasma folate levels. There is a suggestion of a possible positive association between tea drinking and plasma folate concentrations.

The English in this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see http://www.textcheck.com/certificate/wHiXXd

Acknowledgements

Acknowledgements: The authors would like to thank the official support from the Department of Maternal and Child Health of National health commission of People's Republic of China. We are grateful to all study participants and the many health care workers involved from project sites in Inner Mongolia, Gansu, Liaoning, Shandong, Sichuan, Guangdong, Xinjiang, Uygur, Guangxi and Hubei in China. The authors also thank all other staff who participated in the project at the Peking University Health Science Center. The authors would like to express gratitude to Dr Bin Wang, who has provided suggestions and revising language for this manuscript. Financial support: This work was supported by WHO - Ministry Of Health (MOH) 2004–2005 Cooperation Project [grant number WP/2004/CHN/RPH/3·4/001] and the National Natural Science Foundation of China [Grant 81673177]. Conflict of interest: None. Authorship: All authors accept responsibility for the paper as published. XJ wrote the manuscript. XJ and MR both contributed to the statistical analysis discussion and reviewed/edited the manuscript. YZ and BW contributed to discussion and reviewed/edited the manuscript.





RY and LZ were involved in the study design, data collection and contributed to discussion. LZ and ZL contributed to discussion and reviewed the manuscript. LZ and XJ were mainly responsible for the revise of this article. Ethical Standards Disclosure: This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the Institutional Review Board of Peking University Health Science Center. Written informed consent was obtained from all subjects.

Supplementary material

For supplementary material accompanying this paper visit https://doi.org/10.1017/S1368980020004851

References

- Geisel J (2003) Folic acid and neural tube defects in pregnancy: a review. J Perinat Neonatal Nurs 17, 268-279.
- Czeizel AE, Dudas I, Vereczkey A et al. (2013) Folate deficiency and folic acid supplementation: the prevention of neural-tube defects and congenital heart defects. Nutrients **5**, 4760-4775
- Khan N & Mukhtar H (2013) Tea and health: studies in humans. Curr Pharm Des 19, 6141-6147.
- Ye R, Ren A, Zhang L et al. (2011) Tea drinking as a risk factor for neural tube defects in northern China. Epidemiology 22,
- Correa A, Stolley A & Liu Y (2000) Prenatal tea consumption and risks of anencephaly and spina bifida. Ann Epidemiol **10**, 476–477.
- Ren A (2011) Research progress on the relationship between tea drinking and the risk of neural tube defects (In Chinese). Chin J Reprod Health 22, 1745.
- Yazdy, MM, Tinker SC, Mitchell AA et al. (2012) Maternal tea consumption during early pregnancy and the risk of spina bifida. Birth Defects Res A Clin Mol Teratol 94, 756-761.
- Augustin K, Frank J, Augustin S et al. (2009) Greeen tea extracts lower serum folates in rats at very high dietary concentrations only and do not affect plasma folates in a human pilot study. J physiol pharmacol: official J Polish Physiol Soc J Physiol Pharmacol 60, 103-108.
- Alemdaroglu NC, Dietz U, Wolffram S et al. (2008) Influence of green and black tea on folic acid pharmacokinetics in healthy volunteers: potential risk of diminished folic acid bioavailability. Biopharm Drug Dispos 29, 335-348.
- 10. Liu J, Jin L, Zhang Y et al. (2015) Tea consumption is not associated with reduced plasma folate concentration among Chinese pregnant women. Birth Defects Res A Clin Mol Teratol 103, 747–753.
- Zhao Y, Hao L, Zhang L et al. (2009) Plasma folate status and dietary folate intake among Chinese women of childbearing age. Matern Child Nutr 5, 104–116.
- Yang YX (2005) Chinese Food Composition, 2004. Beijing: Peking University Medical Press.

- Shiraishi M, Haruna M, Matsuzaki M et al. (2010) Association between the serum folate levels and tea consumption during pregnancy. Biosci Trends 4, 225-230.
- 14. Chen C & Lu FC (2004) The guidelines for prevention and control of overweight and obesity in Chinese adults. Biomed Environ Sci 17, 1–36.
- 15. Stahl WH (1963) The chemistry of tea and tea manufacturing. Adv Food Res 11, 201-262.
- 16. O'Broin S & Kelleher B (1992) Microbiological assay on microtitre plates of folate in serum and red cells. J Clin Pathol 45, 344-347.
- 17. Hao L, Ma J, Stampfer MJ et al. (2003) Geographical, seasonal and gender differences in folate status among Chinese adults. J Nutr 133, 3630-3635.
- Adhami VM, Ahmad N & Mukhtar H (2003) Molecular targets for green tea in prostate cancer prevention. J Nutr 133, 2417s-2424s.
- Thakur VS, Gupta K & Gupta S (2012) The chemopreventive and chemotherapeutic potentials of tea polyphenols. Curr Pharm Biotechnol 13, 191-199.
- Arab L, Khan F & Lam H (2013) Tea consumption and cardiovascular disease risk. Am J Clin Nutr 98, 1651s-1659s.
- 21. Zhang C, Qin YY, Wei X et al. (2015) Tea consumption and risk of cardiovascular outcomes and total mortality: a systematic review and meta-analysis of prospective observational studies. Eur J Epidemiol 30, 103-113.
- 22. Dutta D & Mohanakumar KP (2015) Tea and Parkinson's disease: constituents of tea synergize with antiparkinsonian drugs to provide better therapeutic benefits. Neurochem Int 89, 181-190.
- Li X, Lyu J, Guo Y et al. (2015) Regional differences in adults' tea drinking pattern: findings from China Kadoorie Biobank study in 10 areas in China (In Chinese). Chin J Epidemiol 36, 1195-1199
- Centers for Disease Control and Prevention (CDC) (2007) Folate status in women of childbearing age, by race/ethnicity-United States, 1999-2000, 2001-2002, and 2003-2004. MMWR 55, 1377-1380.
- McKay DL & Blumberg JB (2002) The role of tea in human health: an update. J Am Coll Nutr 21, 1-13.
- Lin L & Wang XJ (2010) Study on the Relationship between Dietary Folate Intake and Blood Folate Levels in Women of Childbearing Age (In Chinese). Taiyuan: The Summit of Perinatal Medicine.
- Chen TS, Lui CK & Smith CH (1983) Folacin content of tea. J Am Diet Assoc **82**, 627–632.
- Stagg GV & Millin DJ (1975) The nutritional and therapeutic value of tea: a review. J Sci Fd Agric 26, 1439-1459.
- Rasmussen LB, Ovesen L, Bulow I et al. (2000) Folate intake, lifestyle factors, and homocysteine concentrations in younger and older women. Am J Clin Nutr 72, 1156-1163.
- Hodgson JM, Devine A, Puddey IB et al. (2006) Drinking tea is associated with lower plasma total homocysteine in older women. Asia Pac J Clin Nutr 15, 253-258.
- 31. Chen P & Pan BS (2016) Clinical application of serum folate and red blood cell folate determinations (In Chinese). Lab Med 31, 232-236.
- Neuhouser ML, Cheng TY, Beresford SA et al. (2015) Red blood cell folate and plasma folate are not associated with risk of incident colorectal cancer in the Women's Health Initiative observational study. Int J Cancer 137, 930-939.

