Original Article

Habitual tea drinking associated with a lower risk of type 2 diabetes in Vietnamese adults

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Background and Objectives: The association between tea consumption and type 2 diabetes risk remains inconsistent in Asian populations. This case-control study investigated the association between habitual tea consumption and the risk of type 2 diabetes among Vietnamese adults. **Methods and Study Design:** A hospital-based case-control study was conducted during 2013-2015 in Vietnam. A total of 599 newly diagnosed diabetic cases (aged 40-65 years) and 599 hospital-based controls, frequency matched by age and sex, were recruited. Information about frequency, quantity, and duration of tea drinking, together with demographics, habitual diet and lifestyle characteristics, was obtained from direct interviews using a validated and reliable questionnaire. Unconditional logistic regression analyses were performed to assess the association between different metrics of tea consumption and the type 2 diabetes risk. **Results:** Control subjects reported higher tea consumption levels than the cases in terms of duration, frequency, and quantity of tea drunk. After accounting for confounding factors, increasing tea consumption was found to be associated with a reduced risk of type 2 diabetes; the adjusted odds ratio (95% confidence interval) was 0.66 (0.49, 0.89) for participants drinking >2 cups/day, relative to those drinking <1 cup/day. Significant inverse dose-response relationships were also observed for average number of cups consumed daily and years of tea drinking (p<0.01). **Conclusions:** Habitual tea consumption is associated with a reduced risk of type 2 diabetes among Vietnamese adults.

Key Words: case-control study, green tea, tea consumption, risk factors, type 2 diabetes

INTRODUCTION

The number of people with type 2 diabetes (T2D) has increased substantially over the past decade,[1] with an estimated 415 million adults with diabetes worldwide in 2015. Particularly, the Western Pacific region alone accounted for about 37% (~ 154 million).[2] T2D is known to inflict serious morbidities and complications related to cardiovascular diseases[3] and premature deaths, causing enormous burden on the society and the health care system.[4]

Along with increasing physical activity, an appropriate diet and nutritional intake have been advocated for the management and prevention of T2D.[5-7] In particular, the beneficial role of antioxidant-rich foods and beverages has received much attention.[8,9] Tea, especially green tea, is widely consumed in Asia.[10] It contains many bioactive compounds such as catechins[9] and polyphenols,[11] which have been demonstrated to increase insulin sensitivity and prevent glucose metabolism disorder among in vitro and in vivo studies.[12-14] However, the available epidemiological evidence regarding the effect of green tea against T2D development remains inconsistent.[15,16] A systematic review and meta-analysis of nine cohort studies found that all tea (i.e. without specification of types) consumption could significantly lower the T2D risk,[17] whereas few studies have investigated the association between green tea and T2D, showing a lack of association.[15] Moreover, clinical trials have still yielded mixed results for the effect of green tea on hyperglycemia and insulin resistance,[18-21] two precursors to T2D. In view of the different types of tea and variations in consumption pattern between countries, further epidemiological studies are needed to clarify the causal relationships with the T2D risk.

Vietnam is one of the largest tea producing countries in the world.[22] The prevalence of diabetes in Vietnam has doubled from 2.7% in 2002 to 5.4% in 2012,[23,24] which may be attributed to advancing age, overweight/obesity, and a sedentary lifestyle.[25] Because T2D is often asymptomatic at onset and can remain undiagnosed for several years, the disease is typically diagnosed at its advanced stage. In addition, despite the popularity of tea, especially green tea, no epidemiological study of tea and T2D has been conducted in Vietnam. Therefore, the present case-

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Manuscript received 23 November 2016. Initial review completed 06 January 2017. Revision accepted 13 March 2017.
doi: 10.6133/apjcn.072017.08

control study investigated the association between habitual tea consumption and the risk of T2D among Vietnamese adults.

METHODS

Study design and patients

A case-control study was conducted between August 2013 and October 2015. Details of the study design and methodology were described elsewhere.[26] Briefly, patients aged 40-65 years with newly diagnosed T2D were recruited from the Endocrinology Department of a general hospital in Hanoi, capital city of Vietnam. Controls were selected from individuals seeking medical care at outpatient departments of the same hospital, who were frequency-matched to cases on sex and age (±3 years) on a 1:1 ratio. Their diabetic-free status was verified by physicians and checking against plasma glucose records. Eligible consented controls were then interviewed using the same questionnaire as the cases. Inclusion criteria for controls were (1) individuals who attended hospital outpatient departments including ophthalmology, ear-nose-throat and dentistry due to minor health problems; (2) whose plasma glucose levels fell within the normal range according to the WHO diagnostic criteria 2006 [i.e. fasting plasma glucose <7.0 mmol/L (126 mg/dL) or 2–h plasma glucose <11.1 mmol/L (200 mg/dL)]; and (3) at the same age group as cases (±3 years).

Cases of T2D were determined by physicians who directly examined and treated patients through fasting glucose and/or 2-h oral glucose tolerance test. Similarly, all potential controls undertook such testing on the day of their outpatient clinic visit. A total of 599 incident T2D cases (diagnosed within four weeks) and 599 eligible controls were recruited during the same period of data collection. All patients agreed to participate in the study.

Interview and ethics

A trained interviewer used the same questionnaire to interview all participants after obtaining their signed informed consent. Each interview took about 40 minutes to complete. The interview was conducted in a private room at the hospital to maximise the accuracy of information collected. All participants were blinded to the study hypothesis. The interviewer followed a standardized protocol for the interview procedure. The study was approved by the Human Research Ethics Committee of Curtin University (approval number: HR105/2013). Recruitment and access to medical records were permitted by the hospital authority.

Questionnaire and exposure measurement

A structured questionnaire was administered to obtain information on socio-demographic characteristics, family history of diabetes, dietary habits, and lifestyle (physical activity, lifetime alcohol consumption, and cigarette smoking), via personal interview and medical record retrieval. Habitual dietary intakes were assessed using a validated food frequency questionnaire.[27] It consisted of 128 common food and beverage items, seeking detailed information on frequency and amount of intake. The recall period for dietary habits was set to one year before the interview. A picture booklet was used to assist participants in estimating the intake amount and portion size of certain food items. Total energy intake was calculated by summing energy intakes across individual food and beverage items consumed based on the Vietnamese Food Composition Tables.[28] As for tea drinking, participants reported the frequency (times per day, week, month or year) and quantity per session (number of cups), together with the type of tea consumed (green tea, black tea or oolong tea) and duration of drinking (years). A standard 100 ml cup was used for quantifying the amount of tea consumed. Any change in tea drinking habit was also recorded.

Clinical data extraction and measurements

Clinical and biochemical laboratory results, including lipid profile and plasma glucose level, were extracted from patient log-books or medical records. Anthropometric measurements, such as height, weight, waist and hip circumferences, were measured using standard instruments and protocols.[26] Blood pressure and pulse rate were also taken twice after the participant had rested for at least five minutes. Hypertension was defined as a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mmHg.

Statistical analysis

Characteristics between case and control groups, especially habitual tea consumption levels, were compared using chi-square, two-sample t-test or Wilcoxon rank-sum test. To determine the association between tea drinking exposure and T2D risk, separate unconditional logistic regression analyses were performed for tea drinking (yes, no), average tea consumption (<1, 1-2, >2 cups/day) and duration of drinking (<5, 5-10, >10 years), with the respective lowest level being taken as the reference category. Both crude and adjusted odds ratios (OR) and associated 95% confidence intervals (CI) were presented, and tests for linear trend were conducted to ascertain the dose-response relationship, by treating the tea consumption level or drinking duration as a continuous variable in the logistic regression models. However, analysis by tea type was not undertaken because of the mixed tea drinking habit. In fact, 87.5% of the participants drank both green tea and black tea and 100% drank a combination of green tea and oolong tea.

Besides tea drinking variables, independent factors included in the logistic regression models were age at interview (years), sex (female, male), body mass index (kg/m^2), waist-hip ratio, education level (primary/secondary school, tertiary), total energy intake (kcal/day), lifetime coffee drinking (yes, no), lifetime alcohol consumption (yes, no), cigarette smoking (never, former, current), lifetime physical activity (never active, active), first-degree family history of diabetes (yes, no), hypertension (yes, no), and total cholesterol (mmol/L). These confounding variables were either established or plausible risk factors according to the literature.[17,29,32,33] All statistical analyses were performed using Stata 12.0 (StataCorp LP, College Station, TX). A two-sided p value <0.05 was considered statistically significant.

RESULTS

Table 1 shows characteristics of the sample by case-control status. Participants were about 58 years of age on average (SD 7 years). The T2D patients had higher BMI, WHR, fasting blood glucose level, total energy intake and prevalence of hypertension, but lower educational level, lower total plasma cholesterol level, and less physical activity than their control counterparts. The two groups were similar in terms of lifetime alcohol consumption and smoking. First-degree family history of diabetes was three-fold higher in the case group than the controls.

Table 2 compares the tea consumption patterns between case and control groups. Among the tea drinkers, the control patients drank more tea on average per day. In addition, their duration of tea drinking was also significantly longer than the T2D patients.

Figure 1 summaries the results of logistic regression analyses. Collinearity diagnostics, such as variance inflation factors, suggested that the apparent correlation between confounding variables did not pose any problem in the estimation of model parameters. It is evident that tea drinking was associated with a reduced odds of T2D after adjustment of confounding factors (adjusted OR 0.75, 95% CI: 0.57, 1.00). There was also a significant inverse association between levels of habitual tea drinking and the T2D risk. The adjusted OR (95% CI) was 0.66 (0.49, 0.89) among those drinking >2 cups/day compared to <1 cup/day. A similar T2D risk reduction was observed for long-term tea drinking over 10 years relative to those drinking less than 5 years. Finally, potential non-linearity of the dose-response relationship was examined using restricted cubic splines with three knots (50, 75 and 95) via the Stata 'mkspline' command. We found no evidence of non-linear association between tea drinking and risk of T2D (p=0.13).

DISCUSSION

The present case-control study was the first epidemiological investigation of habitual tea drinking in relation to the risk of T2D in Vietnam. Our finding of an inverse association between tea consumption level and the T2D risk is generally consistent with previous observational studies in other countries.[17,29,30,31] In addition, some clinical trials have shown that green tea consumption improves glucose tolerance[32] and insulin resistance,[33] two important preconditions for T2D. Therefore, the present study provides further evidence to support the protective effect of habitual tea drinking against the development of T2D.

However, some previous cohort studies found a lack of association between consumption of green tea[15] or tea[34] with the T2D risk. This may be partly due to their reliance on baseline assessment of tea drinking, despite the

Table 1. Characteristics of participants by case-control status

Characteristics	Cases (n=599)	Controls (n=599)	p value
Age at interview (years): mean±SD	58.6±6.5	58.3±6.6	>0.05*
Female: n (%)	324 (54.0)	324 (54.0)	>0.05†
Body mass index (kg/m^2): mean±SD	23.5±3.2	22.7±2.9	<0.01*
Waist-hip ratio: mean±SD	0.91±0.06	0.89±0.06	<0.01*
Education level: n (%)			<0.01†
Primary/secondary school	283 (47.2)	169 (28.2)	
Tertiary	316 (52.8)	430 (71.8)	
Total energy intake (kcal/day): mean±SD	1532±565	1330±474	<0.01*
Lifetime coffee drinking: n (%)	145 (24.2)	192 (32.0)	<0.01†
Lifetime alcohol consumption: n (%)	275 (45.9)	253 (42.2)	0.20†
Cigarette smoking: n (%)		15	0.05†
Never	408 (68.1)	444 (74.1)	
Former	100 (16.7)	88 (14.7)	
Current	91 (15.2)	67 (11.2)	
Lifetime physical activity: n (%)			<0.01†
Never active	363 (60.0)	282 (47.0)	
Active	236 (40.0)	317 (53.0)	
First-degree family history of diabetes: n (%)	158 (26.4)	56 (9.3)	<0.01†
Hypertension: n (%)	121 (20.2)	90 (15.0)	<0.05†
Total cholesterol (mmol/L): mean±SD	5.4 (1.5)	5.6 (1.2)	0.016*
Fasting glucose level (mmol/L): mean±SD	9.12±5.10	5.50±0.64	<0.01*

SD: standard deviation.
† From chi-square or *t-test between case and control groups.

Table 2. Comparison of tea consumption levels among tea drinkers between case and control groups

Tea consumption variables	Cases (n=334)	Controls (n=373)	p value†
	Mean±SD	Mean±SD	
Quantity of tea drank (mL per day)	318±233	392±355	0.001
Average amount of tea consumption (cups per day)	1.2±1.5	1.5±2.0	0.001
Duration of tea drinking (years)	7.6±9.2	9.7±11.9	0.001

SD: standard deviation.
†From t-test between case and control groups.

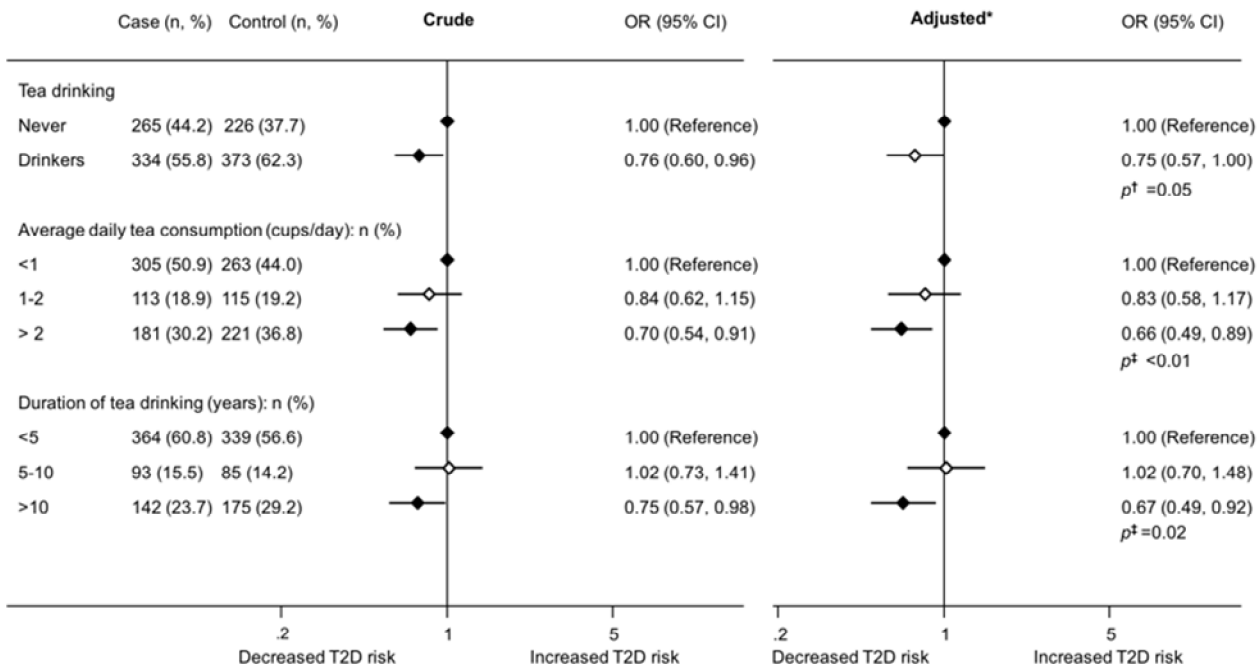

Figure 1. Crude and multivariate-adjusted odds ratios of type 2 diabetes by different measures of tea consumption. The diamond indicates the point estimates and the bar represents the 95% confidence interval. Filled diamonds denotes statistical significance compared to non-drinkers or the lowest category of tea consumption. *Variables adjusted for included for age at interview (years), sex (female, male), body mass index (kg/m^2), waist-hip ratio, education level (primary/secondary school, tertiary), total energy intake (kcal/day), lifetime coffee drinking (yes, no), lifetime alcohol consumption (yes, no), cigarette smoking (never, former, current), lifetime physical activity (never active, active), first-degree family history of diabetes (yes, no), hypertension (yes, no), and total cholesterol (mmol/L). †From chi-square. ‡From test for linear trend. CI: confidence interval; OR: odds ratio; T2D: type 2 diabetes.

tea consumption level and habit can change over the life course. Alternatively, tea drinking assessed prospectively can be non-differentially misclassified, leading to a dilution of statistical association. The discrepancy between our result and some previous studies[15,34] may be attributed to the differences in tea types, preparation methods and drinking habits between cultures. Green tea is the most popular type of tea drunk by Vietnamese adults. It contains a much higher level of catechins than black tea,[11] particularly epigallocatechin-3-gallate (EGCG), which have been shown to increase the action of insulin in rat models.[19] Another possibility is the different methods of manufacture, processing and strength of tea brewed, which can affect the composition of tea infusion.[35] It is conceivable that Vietnamese adults typically drink hot and strong green tea brewed directly from tea leaves without adding sugar or milk, thereby increasing the bioavailability and antioxidant activity of tea polyphenols.

T2D has a relatively long latency period,[36] and therefore it may take years of tea drinking for effective disease prevention. A recent meta-analysis reported that an inverse association between tea consumption and T2D risk was observed only among cohort studies with over 10 years of follow-up.[33] In line with such a meta-analysis, we found significantly lower odds of T2D among participants who drank tea regularly for over 10 years, when compared to others with less than 5 years of drinking history. Our results suggest that, besides the quantity of tea drinking, a long duration of regular tea consumption may be associated with a lower risk of T2D.

There are plausible biological mechanisms underlying the beneficial effect of habitual tea consumption. First, tea catechins, particularly EGCG, can increase insulin sensitivity by augmenting insulin-stimulated glucose uptake in adipocytes[19] and improve insulin resistance through ameliorating impaired insulin signalling due to elevated glucose in HepG2 cells.[37] Second, tea catechins can decrease glucose production in the gastrointestinal system by inhibiting several carbohydrate digestive enzymes,[38,39] thereby lowering circulating levels of glucose and insulin. Third, green tea supplementation has been suggested to protect against pancreatic beta-cells' injury.[12] Finally, subclinical inflammation has been implicated in the pathogenesis of T2D,[40] while tea consumption has been demonstrated to reduce C-reactive protein,[41] the best biomarker of low-grade inflammation.

Several limitations should be mentioned. First, a cause-effect relationship between tea drinking and T2D may not be established due to the retrospective cross-sectional design. Second, the controls were not recruited from the general population. Therefore, to minimise selection bias, we selected control subjects who came from the same catchment area, sought medical care due to non-metabolic conditions, and frequency matched to the cases by age and sex. Third, recall bias may lead to spurious associations between exposures (tea drinking history) and the outcome of interest (T2D).[42] In this study, the direct interview of both case and control groups by the same trained interviewer should help to reduce recall bias and improve the accuracy of information obtained. Moreover, a consistent inverse association with the T2D risk was evident for various measures of tea consumption, even though the effects of different tea types could not be distinguished because of the mixed tea drinking habits of the

Vietnamese adults. In fact, green tea accounted for approximately 99% of consumption among the tea drinkers. Finally, our findings cannot be generalised to the entire Vietnamese population despite all participants were recruited from the same catchment area within metropolitan Hanoi city.

In conclusion, our study showed an inverse association between habitual tea consumption and risk of T2D among Vietnamese adults. The observed evidence provides further support concerning the benefits of cumulative green tea consumption, especially over the long term, for potential prevention and control of this emerging disease in Vietnam. However, replications of the present study in other locations and large-scale clinical trials are essential to confirm the findings.

ACKNOWLEDGEMENTS

The authors are indebted to the study participants who agreed to be interviewed. Thanks are also due to the medical, nursing, and laboratory staff of Thanh Nhan Hospital for their assistance in patient recruitment and data collection.

AUTHOR DISCLOSURES

The authors have no conflict of interest to declare. The study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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