Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Short Communication

Green tea consumption and SARS-CoV-2 infection among staff of a referral hospital in Japan

Akiko Nanri a, b, *, Shohei Yamamoto b, Maki Konishi b, Norio Ohmagari c, Tetsuya Mizoue b

a Department of Food and Health Sciences, International College of Arts and Sciences, Fukuoka Women’s University, 1-1-1 Kasumigaoka, Higashi-ku, Fukuoka, 813-8529, Japan
b Department of Epidemiology and Prevention, Center for Clinical Sciences, National Center for Global Health and Medicine, 1-21-1 Toyama, Shinjuku-ku, Tokyo, 162-8655, Japan
c Disease Control and Prevention Center, National Center for Global Health and Medicine, 1-21-1 Toyama, Shinjuku-ku, Tokyo, 162-8655, Japan

ARTICLE INFO

Article history:
Received 20 November 2021
Accepted 10 January 2022
Available online 13 January 2022

Keywords:
Coronavirus disease
Green tea
Japanese
SARS-CoV-2

SUMMARY

Background & Aim: This study examined the association between green tea consumption and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among Japanese.

Methods: Participants were staff of a large referral hospital in Tokyo. Green tea consumption was ascertained via a questionnaire. SARS-CoV-2 infection was identified through in-house records of PCR-confirmed COVID-19 cases or antibody tests. Multiple logistic regression was used to estimate the odds ratio of SARS-CoV-2 infection according to green tea consumption.

Results: Of 2640 participants (767 men and 1873 women; aged 21–75 years), 74 (2.8%) were confirmed or suspected to have been infected with SARS-CoV-2 during the epidemic. Overall, SARS-CoV-2 infection was not significantly associated with green tea consumption. There was a suggestion of a decrease in the odds of this infection associated with green tea consumption of ≥4 cups/day (odds ratio 0.51, 95% confidence interval 0.20–1.31).

Conclusions: Green tea consumption was not appreciably associated with the risk of SARS-CoV-2 infection. A lower odds of

* Corresponding author. Department of Food and Health Sciences, International College of Arts and Sciences, Fukuoka Women’s University, 1-1-1 Kasumigaoka, Higashi-ku, Fukuoka, 813-8529, Japan.
E-mail address: nanri@fwu.ac.jp (A. Nanri).
1. Introduction

The pandemic of coronavirus disease (COVID-19) has led to 241.9 million patients and 4.9 million deaths globally as of October 21, 2021 [1]. WHO has recommended infection prevention behaviors, including physical distancing and use of mask as well as vaccination [2]. Green tea has been suggested to lower the risk of influenza and upper respiratory tract infections [3]. Experimental studies show that epigallocatechin gallate, rich in green tea, inhibits infection and transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [4,5]. Countries with higher consumption of green tea are shown to have a lower morbidity/mortality rate of COVID-19 [6]. Here we examined the association of green tea consumption with COVID-19 infection in a cohort of healthcare workers in Japan.

2. Methods

The present study used data of ongoing repeat serological survey during the COVID-19 pandemic among workers of the National Center for Global Health and Medicine, Japan (NCGM) [7,8]. Participants were asked to donate venous blood and answer a questionnaire in each survey. We measured IgG (Abbott ARCHITECT®) and total antibodies (Roche Elecsys®) against the SARS-CoV-2 nucleocapsid (N) protein. Written informed consent was obtained from each participant. This study was approved by the ethics committee of NCGM. Green tea consumption was asked at the third survey, in which 2,779 participated (90%). Of these, we excluded those who lacked data necessary for the analysis, leaving 2,640 aged 21–75 years (767 men and 1,873 women) for analysis. We defined SARS-CoV-2 infection using two sources of information: the above-mentioned antibody tests (positive on either test at least once in the three surveys) and in-house records of PCR-confirmed COVID-19 cases. We asked about green tea consumption over the last month with six options ranging from “none or <2 day/week” to “≥4 cups/day” and divided participants into four (“<1 cup/day” to “≥4 cups/day”).

Baseline characteristics according to green tea consumption were expressed as mean (standard deviation) for continuous variables and percentage for categorical variables. Trend association between confounding factors and green tea consumption were tested using linear regression analysis for continuous variables, treating ordinal number in each category of green tea consumption as a continuous variable, and the Mantel-Haenszel chi-squared test for categorical variables. We run multiple logistic regression to estimate odds ratios of SARS-CoV-2 infection for green tea consumption with adjustment for age, sex, occupation, occupational risk of SARS-CoV-2 infection, infection prevention practice, body mass index (BMI), use of public transportation, high-risk behavior (2 items), and close contact with COVID-19 patient. Trend association was assessed by assigning ordinal numbers to the increasing category of green tea consumption and treating them as continuous. We repeated the analysis by information source (PCR-confirmed or antibody test positive only) and timing of infection (before or after vaccination of Pfizer-BioNTech). Additionally, we performed a sensitivity analysis using dichotomized category of green tea consumption (<2 cups/day and ≥3 cups/day). Two-side P values <0.05 were regarded as statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

3. Results

Baseline characteristics of participants according to category of green tea consumption are shown in Table 1. Participants with higher consumption of green tea tended to have higher BMI and use public
transportation (train or bus) compared to those with lower consumption. No other differences according to green tea consumption were observed.

A total of 40 participants, including 19 who completed the second dose of vaccination, were identified through in-house records as having contracted with COVID-19. Of the remaining cases, 34 were positive on at least one SARS-CoV-2 antibody test. A total of 1049 (39.7%) drank green tea on a daily basis. Overall, there was no significant association between green tea consumption and SARS-CoV-2 infection (Table 2). However, there was a suggestion of decreased odds of SARS-CoV-2 infection associated with green tea consumption of ≥4 cups/day (multivariable-adjusted odds ratio 0.51, 95% confidence interval 0.20–1.31). The decreased, albeit not statistically significant, odds ratio associated with green tea consumption of ≥4 cups/day was observed for PCR-confirmed SARS-CoV-2 infection (multivariable-adjusted odds ratio 0.36, 95% confidence interval 0.08–1.58), antibody test-suggested SARS-CoV-2 infection (0.72, 0.21–2.44), COVID-19 diagnosed before vaccination (0.28, 0.04–2.24), and COVID-19 diagnosed after vaccination (0.46, 0.06–3.71).

Sensitivity analysis using dichotomized categories of green tea consumption showed similar results; the multivariable-adjusted odds ratios (95% confidence interval) of green tea consumption of ≥4 cups/day versus ≤2 cups/day were 0.62 (0.33–1.18) for SARS-CoV-2 infection, 0.64 (0.27–1.49) for SARS-CoV-2 infection confirmed with PCR, 0.60 (0.23–1.58) for antibody test-suggested SARS-CoV-2 infection, 0.44 (0.12–1.58) for COVID-19 diagnosed before vaccination, and 0.87 (0.28–2.68) for COVID-19 diagnosed after vaccination.

4. Discussion

In this study among healthcare workers in Japan, where green tea drinking is popular, there was no evidence of a significant association between green tea consumption and SARS-CoV-2 infection, which was confirmed by PCR or suggested by antibody tests. Nevertheless, people who consumed ≥4 cups/day...
day of green tea had a lower, albeit statistically not significant, odds of SARS-CoV-2 infection, a finding compatible with experimental data showing that epigallocatechin gallate inhibits infection and transmission of SARS-CoV-2 [4,5].

The lower odds of infection associated with high green tea consumption was similarly observed across different outcomes (PCR-confirmed or antibody test positive only) and timings (infection before or after vaccination). This finding suggests green tea consumption prevents both symptomatic or asymptomatic infection, irrespectively of vaccination status. Experimental study shows that green tea can inhibit the infection of both wild-type SARS-CoV-2 and its variants with similar magnitude [4]. As the post-vaccination period of the present study corresponded to the epidemic of the Delta variant, the result may also give some support for the effect of green tea against the variant.

The present study was not large enough to detect the observed association with statistical significance. Large-scale investigations are required to confirm the present findings and to explore minimal consumption of green tea associated with lower risk of SARS-CoV-2 infection.

5. Conclusion

The present study did not find significant evidence to support a protective role of green tea consumption against SARS-CoV-2 infection among Japanese. A lower odds of infection among those with high consumption deserves further investigation.
Funding statement

This work was supported by the NCGM COVID-19 Gift Fund [grant number 19K059] and the Japan Health Research Promotion Bureau Research Fund [grant number 2020-B-09].

Author contributions

TM and SY designed the research; NO supervised the research; SY, MK, and TM conducted the survey; AN performed statistical analysis; TM provided statistical expertise; AN drafted the manuscript; AN and TM had primary responsibility for the final content; and all authors approved the final version of the manuscript.

Declaration of competing interest

Abbott Japan and Roche Diagnostics provided reagents for anti-spike antibody assays.

Acknowledgments

We thank Haruka Osawa and Mika Shichishima for their contribution to data collection and the staff of the Laboratory Testing Department for their contribution to measuring antibody testing.

References

[1] World Health Organization. WHO Coronavirus (COVID-19) Dashboard. (Accessed October 21, 2021, at https://covid19.who.int/).
[2] World Health Organization. Coronavirus disease (COVID-19) Prevention. (Accessed September 28, 2021, at https://www.who.int/health-topics/coronavirus#tab_2).
[3] Umeda M, Tominaga T, Kozuma K, Kitazawa H, Furushima D, Hibi M, et al. Preventive effects of tea and tea catechins against influenza and acute upper respiratory tract infections: a systematic review and meta-analysis. Eur J Nutr 2021;60:4189-202.
[4] Liu J, Bodnar BH, Meng F, Khan AI, Wang X, Saribas S, et al. Epigallocatechin gallate from green tea effectively blocks infection of SARS-CoV-2 and new variants by inhibiting spike binding to ACE2 receptor. Cell Biosci 2021;11:168.
[5] Henss L, Auste A, Schürmann C, Schmidt C, von Rhein C, Mühlebach MD, et al. The green tea catechin epigallocatechin gallate inhibits SARS-CoV-2 infection. J Gen Virol 2021;102:001574.
[6] Storozhuk M. COVID-19: could green tea catechins reduce the risks? medRxiv 2021. https://doi.org/10.1101/2020.10.23.20218479.
[7] Tanaka A, Yamamoto S, Miyo K, Mizoue T, Maeda K, Sugiuira W, et al. Seroprevalence of antibodies against SARS-CoV-2 in a large national hospital and affiliated facility in Tokyo, Japan. J Infect 2021;82(4):e1–3.
[8] Yamamoto S, Tanaka A, Oshiro Y, Ishii M, Ishiwari H, Konishi M, et al. Seroprevalence of SARS-CoV-2 antibodies in a national hospital and affiliated facility after the second epidemic wave of Japan. J Infect 2021;83(2):237–79.