Original Article

Does tea consumption during early pregnancy have an adverse effect on birth outcomes?

Jin-Hua Lu[1,*], Jian-Rong He[1,*], Song-Ying Shen [1], Xue-Ling Wei[1], Nian-Nian Chen[1], Ming-Yang Yuan[1], Lan Qiu[1], Wei-Dong Li[1], Qiao-Zhu Chen[2], Cui-Yue Hu[1], Hui-Min Xia[1], Suzanne Bartington[3], Kar Keung Cheng[3], Kin Bong Hubert Lam[4,†], Xiu Qiu[1,†] on behalf of the Born in Guangzhou Cohort Study Group

[1] Division of Birth Cohort Study, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangzhou, China

[2] Department of Obstetrics and Gynecology, Guangzhou Women and Children Medical Center, Guangzhou Medical University, Guangzhou, China

[3] Institute of Applied Health Research, University of Birmingham, Birmingham, UK

[4] Nuffield Department of Population Health, University of Oxford, Oxford, UK

* These authors contributed equally to this work.

†To whom correspondence should be addressed.

Dr Xiu Qiu, Division of Birth Cohort Study, Guangzhou Women and Children's Medical Center, 9 Junsui Road, Zhujiang Newtown, Tianhe District, Guangzhou 510623, China, Tel/Fax: +86 20 38367162, e-mail: qxiu0161@163.com

Dr Kin Bong Hubert Lam, Nuffield Department of Population Health, University of Oxford, Richard Doll Building, Old Road Campus, Oxford OX3 7LF, UK, Tel: +44 0 1865 743621 Fax: +44 0 1865 743980, e-mail: hubert.lam@ndph.ox.ac.uk

Running title: Tea consumption and birth outcomes

Acknowledgements

We are grateful to the participants of the BIGCS study and all obstetric care providers who have assisted us in the implementation of the study. We also wish to thank the Born in Guangzhou Cohort Study Group, including Yong Guo, Yu Liu, Xiaoyan Xia, Yanyan Wu, Wanqing Xiao, Yingfang Wu, Huiyun Xiao, Huihui Liu, Fengjuan Zhou, Yanfei Xing, Lisha Zhu, Xian Liu, Yan Hu, Ying Ma, Jing Ning, Weidong Li, Yan Li, Xingwen Zou, Lin Jiang, Jing Zhao and Yi Hu

Financial Support

The Born in Guangzhou Cohort Study is supported by the Guangzhou Science and Technology Bureau, Guangzhou, China (grant number 2011Y2-00025, 2012J5100038 and 201508030037).

Conflict of Interest

The authors declare that they have no conflicts of interest.

Contributor statement:

JL, JH, SS, NC, MY, LQ, YW, WL, QC, CH, KBHL, and XQ designed and conducted the study, KKC, SB, HX, and XQ advised on the design and directed its implementation; JL, JH, and XW analysed the data; JH, KBHL and XW designed the study's analytical strategy, performed literature review and wrote the paper. XQ and KBHL had primary responsibility for final content. All authors have read and approved the final manuscript.

Word count 3060

Does tea consumption during early pregnancy have an adverse effect on birth outcomes?

Abstract

Background Tea, a common beverage, has been suggested to exhibit a number of health benefits. However, one of its active ingredients, caffeine, has been associated with preterm birth and low birthweight. We investigated whether tea consumption during early pregnancy is associated with an increased risk of preterm birth and abnormal foetal growth.

Methods A total of 8775 pregnant women were included from the Born in Guangzhou Cohort Study. Tea consumption (type, frequency and strength) during their first trimester and social and demographic factors were obtained via questionnaires administered during pregnancy. Information on birth outcomes and complications during pregnancy was obtained from hospital medical records.

Results Overall habitual tea drinking (≥1 serving/week) prevalence among pregnant women was low, at 16%. After adjustment for potential confounding factors (e.g. maternal age, educational level, monthly income) tea drinking during early pregnancy was not associated with an increased risk of preterm birth, small or large for gestational age ($p>0.05$).

Conclusions We did not identify a consistent association between frequency of tea consumption or tea strength and adverse birth outcomes among Chinese pregnant women with low tea consumption. Our findings suggest that occasional tea drinking during pregnancy is not associated with increased risk of preterm birth or abnormal foetal growth. Given the high overall number of annual births in China, our findings have important public health significance.

Keywords: Tea: Preterm birth: Abnormal foetal growth: Chinese: Birth cohort

Introduction

Preterm birth and abnormal foetal growth (including small for gestational age [SGA] and large for gestational age [LGA]) are important predictors of neonatal morbidity and mortality as well as adverse health outcomes in childhood and adulthood (1-3). A recent study in seven regions in China suggests a preterm birth rate of 7.1% in 2011 (4), and data from Guangzhou, the largest city in southern China, indicate the prevalence of SGA and LGA being 8.6% and 8.5%, respectively (5). Whilst the rates are not particularly high compared to those of south Asia (13.3%) and sub-Saharan Africa (12.3%) (6), given the large absolute number of live births in China (12% of global total in 2010) (6), identification of risk factors associated with preterm birth and abnormal foetal growth is of particular public health importance.

Tea is a beverage prepared from the leaves of the plant Camellia sinensis, and contains a number of biologically active constituents, including polyphenols (e.g. catechins) and alkaloids (e.g. caffeine). Tea is broadly classified into green, oolong and black tea according to the degree of enzyme-mediated oxidation (known as fermentation) (7).

There has been some conflicting evidence on the health benefits of tea [8-10], but much less is known about the potential effects of tea drinking during pregnancy on foetal growth and development. In vivo studies in rats suggested black tea(11) or green tea catechin(12) had no effect on the weight of pups, but to our knowledge, no human studies have investigated the effects of tea on preterm birth and birthweight. On the other hand, reports have suggested that one of the active ingredients in tea, caffeine, is negatively associated with birthweight (13-17). This relationship was confirmed in a recent meta-analysis (18), although there was no association with preterm birth (18, 19). It should be noted, however, that tea consumption has a lesser contribution than coffee for total caffeine intake in the Western populations studied (13-17), whereas in China tea remains the most popular beverage (20).

The current Chinese dietary guidelines (21) do not comment on the frequency of intake and the type of tea. As a substantial number of tea drinkers in China are of child-bearing age, clarifying the potential association of tea consumption on gestational age and birthweight is of public health importance. Using data from a large prospective birth cohort in China, we investigated the effect of tea drinking during early pregnancy on foetal growth and preterm birth.

Methods

Recruitment

The Born in Guangzhou Cohort Study (BIGCS) is an ongoing prospective study conducted by the Guangzhou Women and Children's Medical Center (GWCMC), China, which commenced in February 2012. Details of the recruitment can be found elsewhere (22). Briefly, all pregnant women residing within Guangzhou who attended their first routine antenatal examination (usually around week 16) at two campuses of GWCMC, and who intended to remain in Guangzhou with their child for ≥3 years were invited to participate in BIGCS. At baseline recruitment, demographic and socio-economic information were obtained via self-completed questionnaires, as well as data on workplace and home exposures, lifestyle, medical histories, and health status before and during pregnancy. BIGCS has received approval from the Institutional Ethics Committee of GWCMC. All participants gave written informed consent.

For this analysis, data from pregnant women recruited between February 2012 and December 2014 (n = 10277; 73.6% of those eligible) were used. We excluded those who dropped out before delivery (n = 435), or terminated their pregnancies or had stillbirths (n = 111), or had multiple gestation (n = 212), or who had missing delivery data (n = 155), resulting in 9364 singleton births in this report (Figure 1).

Tea consumption

Participants were asked at baseline (around 16 weeks of gestation) whether they regularly consumed tea during pregnancy. Subsequently, participants were asked to specify the type of tea they drank (green, oolong, black [known as "red tea" in China], and dark [a variety of post-fermented tea in China]), how many servings they consumed each type in a typical week (one serving was defined as 150 mL of tea), and the strength of tea (defined subjectively: weak, moderate, strong) they preferred. We grouped the types of teas into green (unfermented), oolong (semi-fermented) and black and dark tea (fermented) teas. Frequency was categorised into <1, 1–3, and >3 servings/week, and tea strength was dichotomised into weak and moderate/strong.

Birth outcomes

Birthweight among other birth outcomes (gestational age, parity, mode of delivery, and foetal sex) were obtained from the Guangzhou Perinatal Health Care and Delivery Surveillance System which records all births within the municipality. Gestational age at birth was determined based on ultrasound examination within the first- or early second-trimester. Preterm birth was defined as delivery before 37 weeks gestation. Those births with gestational age 37 weeks or above were considered as term. SGA and LGA were defined as a gestational age-adjusted birthweight below the 10th and above the 90th percentile, respectively, derived from a local population-based birthweight reference (23). The remaining births were considered as appropriate for gestational age (AGA).

Covariates

From the questionnaire, we derived maternal age (continuous), highest education level and maternal monthly income. Both education level and monthly income category were used as

proxies for socio-economic status. Maternal smoking three months before pregnancy and during pregnancy (number of cigarettes per day) was assessed. Participants were considered to have environmental tobacco smoke exposure if they were either exposed to second-hand smoke at home or at work during early pregnancy. Folic acid supplement use was recorded in the questionnaire. Pre-pregnancy maternal height (cm) and weight (kg) were self-reported at recruitment, from which body mass index (BMI; kg/m2) was derived. Information on complications during the current pregnancy, including pre-eclampsia, pregnancy-induced hypertension, pre-pregnancy hypertension, gestational diabetes and pre-pregnancy diabetes, was obtained from medical records after delivery.

Statistical analysis

Differences in characteristics by frequency of tea consumption during early pregnancy were evaluated using Student's t-test, $\chi 2$ test or Mann-Whitney U test where appropriate. Logistic regression models were constructed in order to assess the relationship between tea consumption during early pregnancy (frequency and strength) and birth outcomes, adjusting for known determinants of foetal growth (maternal age, complications during pregnancy, parity, and foetal sex), as well as potential confounders relating to tea consumption (socio-economic status, exposure to tobacco smoke, and folic acid supplement use) based on evidence from the literature. We also explored the dose-response relationship between tea consumption and risk of adverse pregnancy outcomes, by including frequency of tea drinking as continuous variable into the regression models. We examined the effects of individual types of tea in two ways: (i) we included additional variables indicating other types of tea to take into account the total tea intake, and (ii) we restricted the analysis to those who only consumed one type of tea to avoid contamination bias. We compared distributions of Z-score

of birthweight and gestational age at birth (both continuous) using the Kruskal-Wallis test, among women with different levels of tea consumption (<1, 1–3, and >3 servings/week).

We also examined whether any relationships were modified by maternal pre-pregnancy BMI by including interaction terms in the models. Although previous studies have suggested that caffeine intake is associated with adverse birth outcomes (13-16), the prevalence of habitual coffee drinking (≥1 serving/week) was extremely low in this cohort (0.9%), and hence we did not include coffee consumption as a confounding factor. However, we conducted a sensitivity analysis restricting those included in the analyses to non-coffee drinking participants. All analyses were performed using SAS statistical software version 9.2 (SAS Institute Inc., Cary, NC, USA). A two-tailed p-value of less than 0.05 was considered statistically significant in all statistical analyses.

Results

Of the 9364 eligible singleton pregnancies, 8775 (93.7%) had available information on tea consumption during early pregnancy and were included in the analysis. Those who were excluded were more likely to have a higher educational level and income compared to those included in the final analyses (Supplementary Table 1). Table 1 presents the characteristics of pregnant women at enrolment and selected pregnancy outcomes. In this sample, 1420 women (16.2%) reported drinking tea at least once per week (median 3, interquartile range 2-5) during early pregnancy. Most of the tea-drinking participants (71.8%) consumed only one type of tea (median 2 servings/week), 22.7% two types (4 servings/week), and 4.2% three types (6 servings/week). Those who consumed tea habitually (at least 1 serving per week) were more likely to be slightly older, have a higher educational level, be exposed to second hand tobacco smoke (34.8 vs. 29.7%), have a higher mean (±SD) pre-pregnancy BMI (20.6 ± 2.8 vs. 20.3 ± 2.6 kg/m2) and to be multiparous (14.9 vs. 10.8%) compared to those mothers

who did not consume tea regularly. Overall, there were no significant difference in birthweight and the proportions of SGA and LGA between children whose mothers did or did not consume tea regularly at baseline.

Results of logistic regression of birth outcomes on tea consumption during early pregnancy are presented in Table 2. There was no association between tea consumption during early pregnancy and the birth outcomes we measured (preterm birth, SGA and LGA), after adjustment for potential confounding factors (maternal age, educational level, monthly income, exposure to environmental tobacco smoke and folic intake during early pregnancy, pre-pregnancy BMI, parity, complications during pregnancy and foetal sex). Among the three types of tea examined, frequent green tea consumption was significantly associated with LGA (fully adjusted OR = 1.67; 95% CI, 1.01, 2.75; p=0.045), but non-significant risk estimates were found for preterm birth (0.54; 0.18, 1.63) and SGA (0.57; 0.21, 1.51). We did not observe any statistically meaningful relationship between oolong tea and dark/black tea consumption and birth outcomes. When we included frequency of tea drinking as continuous variable into the regression models, there was also no apparent dose-response relationship between tea consumption and risk of adverse pregnancy outcomes. When we used Z-score of birthweight instead of the binary SGA and LGA variables, we did not see a positive association between green tea consumption and birthweight, although there was a decreasing trend in gestational age at birth among Oolong tea-drinking women (Supplementary Table 2).

Among the regular tea drinkers at baseline, 22.7% and 4.2% consumed two and three or more types of tea, respectively. To avoid potential attenuation of observed effect sizes due to consumption of multiple tea types, we repeated the analysis by restricting to those who reported to drink only one specific type. Overall, the risk estimates for preterm birth, SGA, and LGA were very similar to those obtained from the analysis using the full sample although the confidence intervals were slightly wider (Supplementary Table 3).

We also investigated the possible effects of tea strength (Table 3). Consumption of weak Oolong tea was associated with reduced risk of preterm birth (OR: 0.21; 95% CI: 0.06, 0.76). We did not find significant association between adverse birth outcomes and strength of green or dark/black tea in multivariate analysis.

As tea drinking may be favoured by women who intend to lose weight, we also tested for potential interaction between pre-pregnancy BMI and tea consumption by including an interaction term in the regression model. This, however, did not change the risk estimates (results not shown). Restricting the analysis to non-coffee drinking participants also did not alter the conclusion (results not shown).

Discussion

In a contemporary sample of Chinese pregnant women with low consumption of tea, we did not find evidence suggesting an adverse effect of tea consumption on gestational age or birthweight of offspring after adjusting for potential confounding factors. Although higher consumption of unfermented tea (green tea) was associated with an increased risk of LGA, this finding was of borderline significance, and may be a result of multiple comparisons. As the official Chinese dietary guidelines do not comment on tea intake during gestation (21), pregnant women are likely to consult internet-based information for dietary advice, which often delivers mixed messages without any scientific evidence, and many women might opt to avoid tea drinking altogether. Our findings do not support the need for pregnant women to abstain from tea drinking during early pregnancy, at least when it is consumed at a low to moderate level.

To our knowledge, our study is the first to investigate the effects of tea consumption on birthweight in an Asian setting with a large prospective birth cohort study. Surprisingly, we observed a low prevalence (only 16%) of tea drinking in the study population. In fact, results

from the China Health and Nutrition Survey (CHNS) suggest the prevalence of tea drinking had fallen by 10% between 1993 and 2009 (from 44% to 34%), and that the most prominent decline has occurred in the 18–29 years age group (by about 20%) (20). Another study of 5133 adults from the three largest Chinese cities (Beijing, Shanghai, and Guangzhou) also found a lower prevalence of tea drinking among those 20–29 years (27%) compared to 30-39 years (46%) (24). These figures support our observation that tea drinking is less popular among the younger generation (particularly those of child-bearing age).

Whilst previous studies have attempted to assess the effect of tea consumption in relation to birthweight (13-17), the focus was generally on caffeine intake and not the beverage per se. A small case-control study of 155 women in Beijing, China found an increased risk of SGA associated with tea consumption at least twice a week during pregnancy (25). Potential recall bias and the lack of adjustment for SGA risk factors (e.g., complications during pregnancy, parity) in the analyses may explain the inconsistency with our own findings.

To date there has been no definitive conclusion on whether tea consumption in pregnant women could affect offspring. It is proposed that excessive caffeine intake might be teratogenic (26). However, a recent review by Brent et al. concluded that results from both epidemiological and animal studies suggest caffeine intake is “unlikely to have reproductive and developmental effects” (27). On the other hand, accumulating findings from animal and human studies have pointed to a possible weight reduction effect by tea. Green tea extracts or (-)-epigallocatechin-3-gallate (EGCG), one of the tea catechins, have been shown to reduce weight gain, blood glucose or insulin levels in obese/diabetic animals or those on high-fat diets (28). In humans, a number of small randomised-controlled trials have been conducted, as summarised by two recent meta-analyses (29, 30). Most of the studies included administered green tea or green tea extracts with caffeine in normal weight or overweight individuals and showed weight reduction compared with caffeine-free controls, hence leading to a question of

whether weight loss was an effect of caffeine in tea, or due to a combined effect of caffeine and tea catechins. A meta-analysis demonstrated that while both caffeine alone and the combination of catechins and caffeine increased daily energy expenditure, only the latter could significantly increase fat oxidation (31). A recent Cochrane review further supported this concept, concluding that green tea preparations may induce little loss of weight in obese or overweight adults (9). As maternal glucose and lipid metabolism during pregnancy is highly relevant to the fetal nutrient supply (32, 33), it is entirely plausible that tea (or catechins in combination with caffeine) could have an adverse impact on birthweight. Nevertheless, after adjusting for confounders we did not find compelling evidence that tea consumption was associated with birthweight Z-score, SGA or LGA.

Results from analyses using tea strength as an exposure measure are somewhat inconsistent with those using the frequency of consumption. Firstly it should be noted that the strength of tea is a subjective indicator in this study and could not precisely represent the dose of tea. Additionally, longer steeping time may not only strengthen the flavour, but may also encourage the release of other components as well as contaminants in tea leaves, such as heavy metals (34). This may introduce toxic effects in addition to the potential weight reducing capacity of catechins and caffeine. For example, a recent case-control study in China found an association between drinking strong tea and congenital birth defect (35).

Strengths of this study include the prospective design, which to some extent reduced recall bias. Our population has a low incidence of coffee drinking and this may avoid potential for confounding due to the high caffeine content of coffee. There are also some limitations that should be considered. Tea consumption was investigated only at baseline during early gestation. It is possible that pregnant women could have changed their exposure during later stages of pregnancy, leading to misclassification and regression dilution bias. Despite the relatively large sample size, only 16% of our sample reported drinking tea at least once a

week. The small number of frequent tea drinkers renders the estimates unstable with wide confidence intervals, and we might not have sufficient statistical power to detect a true association. Nevertheless, the opposing directions in the risk estimates for SGA and LGA lend credibility to the findings. Furthermore, tea drinking in China is a social norm and any misclassification is most likely random (rather than systematic or deliberate under- or over-reporting), diluting the effect size towards the null. Although we have controlled for a range of confounders, we acknowledge the possibility of residual and unmeasured confounding due to other potentially relevant variables such as sleep duration and diet during pregnancy. We were unable to specify whether the observed effect was due to components unique to tea, caffeine in tea or caffeine from other sources such as coffee, and to a lesser extent soft drinks and pain killers. However, the prevalence of regular coffee drinking in our sample was extremely low, and given the lower caffeine content in tea (36), we hypothesised that tea drinking should be responsible for the majority of caffeine (and catechin) intake, and therefore our risk estimates were less likely to be confounded by other dietary factors.

Conclusions

Our results do not suggest an adverse effect of tea consumption at a low to moderate level during early pregnancy on preterm birth or abnormal foetal growth among Chinese women. Given the high overall number of annual births (~17 million in 2014) and the relatively low prevalence of tea drinking among pregnant women in China, our findings have important public health significance in the context of other potential health benefits of tea. Future studies are warranted to confirm our findings and to re-examine the dietary guidelines, which currently do not provide guidance to pregnant women about tea drinking.

References

1. Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. Lancet (London, England). 2008;371(9608):261–9.
2. Johnson RC, Schoeni RF. Early-Life Origins of Adult Disease: National Longitudinal Population-Based Study of the United States. American journal of public health. 2011;101(12):2317-24.
3. Schellong K, Schulz S, Harder T, Plagemann A. Birth weight and long-term overweight risk: systematic review and a meta-analysis including 643,902 persons from 66 studies and 26 countries globally. PloS one. 2012;7(10):e47776.
4. Liying Z, Xin W, Yan R, Guanghui L, Yi C, Weiyuan Z. Preterm birth and neonatal mortality in China in 2011. International Journal of Gynecology & Obstetrics. 2014;127(3):243–7.
5. Guo Y, Liu Y, He JR, Xia XY, Mo WJ, Wang P, et al. Changes in birth weight between 2002 and 2012 in Guangzhou, China. PloS one. 2014;9(12):e115703-e.
6. Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet (London, England). 2012;379(9832):2162-72. Epub 2012/06/12.
7. Yang CS, Hong J. Prevention of Chronic Diseases by Tea: Possible Mechanisms and Human Relevance. Annual Review of Nutrition. 2013;33(3):161-81.
8. Boehm K, Borrelli F, Ernst E, Habacher G, Hung SK, Milazzo S, et al. Green tea (Camellia sinensis) for the prevention of cancer. The Cochrane database of systematic reviews. 2009(3):CD005004. Epub 2009/07/10.

9. Jurgens TM, Whelan AM, Kirk S, Foy E. Green tea for weight loss and weight maintenance in overweight or obese adults. Cochrane Database of Systematic Reviews. 2012;12(12):331-3.
10. Hartley L, Flowers N, Clarke A, Stranges S, Hooper L, Rees K. Green and black tea for the primary prevention of cardiovascular disease. Cochrane Database of Systematic Reviews. 2013;6(6):1073-.
11. Ratnasooriya WD, Fernando TS. Effects of Sri Lankan black tea (Camellia sinensis L.) on pregnancy of rats. Basic & Clinical Pharmacology & Toxicology. 2009;105(6):361-5.
12. Morita O, Knapp JF, Tamaki Y, Stump DG, Moore JS, Nemec MD. Effects of green tea catechin on embryo/fetal development in rats. Food & Chemical Toxicology. 2009;47(6):1296–303.
13. IS S, CG V, S H, JB C. Caffeine intake and low birth weight: a population-based case-control study. American Journal of Epidemiology. 1998;147(7):620-7.
14. Grosso LM, Rosenberg KD, Belanger K, Saftlas AF, Leaderer B, Bracken MB. Maternal caffeine intake and intrauterine growth retardation. Epidemiology. 2001;12(4):447-55. Epub 2001/06/29.
15. Bakker R, Steegers EA, Obradov A, Raat H, Hofman A, Jaddoe VW. Maternal caffeine intake from coffee and tea, fetal growth, and the risks of adverse birth outcomes: the Generation R Study. The American journal of clinical nutrition. 2010;91(6):1691-8. Epub 2010/04/30.
16. Sengpiel V, Elind E, Bacelis J, Nilsson S, Grove J, Myhre R, et al. Maternal caffeine intake during pregnancy is associated with birth weight but not with gestational length: results from a large prospective observational cohort study. BMC medicine. 2013;11(1):42.

17. Hoyt AT, Marilyn B, Sandra R, Paul R, Charlotte S. Maternal Caffeine Consumption and Small for Gestational Age Births: Results from a Population-Based Case–Control Study. Maternal & Child Health Journal. 2014;18(6):1540-51.
18. Greenwood DC, Thatcher NJ, Ye J, Garrard L, Keogh G, King LG, et al. Caffeine intake during pregnancy and adverse birth outcomes: a systematic review and dose-response meta-analysis. European journal of epidemiology. 2014;29(10):725-34. Epub 2014/09/03.
19. Maslova E, Bhattacharya S, Lin S-W, Michels KB. Caffeine consumption during pregnancy and risk of preterm birth: a meta-analysis. The American journal of clinical nutrition. 2010;92(5):1120-32.
20. Zhang B, Wen-Wen DU, Wang HJ, Chang SU, Zhang JG, Zhai FY. Tea and Coffee Consumption Status and Trend Among 18 to 49 Years Old Adults in 9 Provinces of China. Food & Nutrition in China. 2011.
21. Ge K. The transition of Chinese dietary guidelines and food guide pagoda. Asia Pacific journal of clinical nutrition. 2011;20(3):439-46. Epub 2011/08/24.
22. He JR, Yuan MY, Chen NN, Lu JH, Hu CY, Mai WB, et al. Maternal dietary patterns and gestational diabetes mellitus: a large prospective cohort study in China. British Journal of Nutrition. 2015;113(8):1-9.
23. Jian-Rong H, Hui-Min X, Yu L, Xiao-Yan X, Wei-Jian M, Ping W, et al. A new birthweight reference in Guangzhou, southern China, and its comparison with the global reference. Archives of disease in childhood. 2014;99:1091-7.
24. Dong Y, Zhang FD, Wang T, Huan-Ling YU, Ling WH, Cai MQ. Tea Drinking Habits among Residents in Beijing, Shanghai, and Guangzhou. Journal of Environmental & Occupational Medicine. 2012.
25. Han J, Gan D, Zhai G, Shi Y. [A case-control study of risk factors of low birth weight at term]. Wei sheng yan jiu= Journal of hygiene research. 2004;33(4):483-5.

26. Executive RCoPoIHS. Clinical practice guideline No.27: Nutrition for pregnancy. 2013; Available from: http://www.rcpi.ie/content/docs/000001/1180_5_media.pdf.
27. Brent RL, Christian MS, Diener RM. Evaluation of the reproductive and developmental risks of caffeine. Birth defects research Part B, Developmental and reproductive toxicology. 2011;92(2):152-87. Epub 2011/03/04.
28. Sae-Tan S, Grove KA, Lambert JD. Weight control and prevention of metabolic syndrome by green tea. Pharmacological Research. 2010;64(2):146–54.
29. Hursel R, Viechtbauer W, Westerterp-Plantenga MS. The effects of green tea on weight loss and weight maintenance: a meta-analysis. International Journal of Obesity. 2009;33(9):956–61.
30. Phung OJ, Baker WL, Matthews LJ, Michael L, Alicia T, Coleman CI. Effect of green tea catechins with or without caffeine on anthropometric measures: a systematic review and meta-analysis. American Journal of Clinical Nutrition. 2010;91(1):73-81.
31. Hursel R, Viechtbauer W, Dulloo AG, Tremblay A, Tappy L, Rumpler W, et al. The effects of catechin rich teas and caffeine on energy expenditure and fat oxidation: a meta-analysis. Obesity Reviews An Official Journal of the International Association for the Study of Obesity. 2011;12(7):e573–e81.
32. Beyerlein A, Schiessl B, Lack N, von Kries R. Associations of gestational weight loss with birth-related outcome: a retrospective cohort study. BJOG : an international journal of obstetrics and gynaecology. 2011;118(1):55-61. Epub 2010/11/09.
33. Catalano PM, Mele L, Landon MB, Ramin SM, Reddy UM, Casey B, et al. Inadequate weight gain in overweight and obese pregnant women: what is the effect on fetal growth? American journal of obstetrics and gynecology. 2014;211(2):137 e1-7. Epub 2014/02/18.
34. Schwalfenberg G, Genuis SJ, Rodushkin I. The Benefits and Risks of Consuming Brewed Tea: Beware of Toxic Element Contamination. Journal of Toxicology. 2013;2013.

345 35. Yang W, Zeng L, Cheng Y, Chen Z, Wang X, Li X, et al. The effects of periconceptional
346 risk factor exposure and micronutrient supplementation on birth defects in shaanxi
347 province in Western china. PloS one. 2012;7(12):83-.
348 36. Chin JM, Merves ML, Goldberger BA, Sampson-Cone A, Cone EJ. Caffeine content of
349 brewed teas. Journal of analytical toxicology. 2008;32(8):702-4. Epub 2008/11/15.

350 Table 1 Characteristics of the mothers and their children by frequency of tea drinking at
351 enrollment in the Born in Guangzhou Cohort Study, 2012-2014 (n=8775)

	Weekly tea consumption		
	<1 serving	≥ 1 serving	*P*-value
	Mean ± SD or No. (%)	*Mean ± SD or No. (%)*	
n	7355	1420	
Demographic and lifestyle			
Maternal age at enrollment (years)	28.8 ± 3.3	29.1 ± 3.5	<0.01
Educational level			
Middle school or below	824 (11.2)	117 (8.2)	
College	1904 (25.9)	333 (23.5)	
Undergraduate	3803 (51.7)	804 (56.6)	
Postgraduate	824 (11.2)	166 (11.7)	<0.01
Monthly income (Yuan [*])			
≤1500	733 (10.2)	143 (10.4)	
1501-4500	2365 (33.0)	414 (30.0)	
4501-9000	2967 (41.3)	591 (42.8)	
≥9001	1111 (15.5)	234 (16.9)	0.15
Missing	179	38	
Pre-pregnancy BMI (kg/m^2)	20.3 ± 2.6	20.6 ± 2.8	<0.01
Missing	121	21	
Environmental tobacco smoke exposure in early pregnancy	2185 (29.7)	493 (34.8)	<0.01
Missing	6	5	
Folic acid intake in early pregnancy	6721 (91.5)	1300 (91.7)	0.79

Missing	7	2	
Pregnancy-related			
Parity			
Primiparous	6562 (89.2)	1208 (85.1)	
Multiparous	791 (10.8)	212 (14.9)	<0.01
Missing	2	0	
Mode of delivery			
Vaginal delivery	4805 (65.5)	888 (62.8)	
Caesarean section	2535 (34.5)	527 (37.2)	0.05
Missing	15	5	
Gestational age at birth (weeks)			
Median [25^{th}, 75^{th} percentile]	39 [38, 40]	39 [38, 40]	0.47
Preterm birth	364 (5.0)	65 (4.6)	0.55
Missing	41	6	
Birthweight (g)	3188 ± 432	3187 ± 422	0.95
Missing	27	5	
Birthweight for gestational age			
SGA	528 (7.2)	96 (6.8)	
AGA	5995 (81.8)	1170 (82.7)	
LGA	791 (10.8)	148 (10.5)	0.77
Missing	41	6	

Data presented as mean ± SD or n (%) unless otherwise specified.

AGA: appropriate for gestational age; BMI: body mass index; LGA: large for gestational age; SGA: small for gestational age.

*: 1 Yuan ≈ US $0.16 (May 2014).

353 Table 2 Relationship between frequency of tea drinking and birth outcomes in the Born in Guangzhou Cohort Study, 2012-2014 (n=8775)

Weekly tea consumption (serving/week)	Preterm birth			SGA			LGA		
	n	OR (95% CI)		N	OR (95% CI)		n	OR (95% CI)	
	(Preterm /term)	Crude	Adjusted *	(SGA /AGA)	Crude	Adjusted *	(LGA /AGA)	Crude	Adjusted *
Any tea									
<1	364/6965	1.00 (Ref.)	1.00 (Ref.)	541/5995	1.00 (Ref.)	1.00 (Ref.)	791/5995	1.00 (Ref.)	1.00 (Ref.)
1-3	36/799	0.86 (0.61, 1.22)	0.86 (0.59, 1.25)	53/697	0.86 (0.64, 1.16)	0.94 (0.70, 1.28)	84/697	0.91 (0.72, 1.16)	0.88 (0.68, 1.13)
>3	27/526	0.98 (0.66, 1.47)	0.88 (0.57, 1.38)	40/451	1.01 (0.72, 1.41)	1.07 (0.75, 1.53)	62/451	1.04 (0.79, 1.37)	0.97 (0.72, 1.30)
p for trend		0.65	0.41		0.67	0.90		0.92	0.51
Green tea									
1-3	18/363	0.95 (0.58, 1.54)	0.80 (0.44, 1.45)	17/328	0.59 (0.36, 0.97)	0.59 (0.33, 1.05)	36/328	0.83 (0.59, 1.18)	0.89 (0.60, 1.34)
>3	5/132	0.73 (0.30, 1.78)	0.54 (0.18, 1.63)	6/108	0.63 (0.28, 1.44)	0.57 (0.21, 1.51)	23/108	1.61 (1.02, 2.55)	1.67 (1.01, 2.75)
p for trend		0.50	0.23		0.03	0.07		0.34	0.19
Oolong tea									
1-3	13/410	0.61 (0.35, 1.06)	0.61 (0.33, 1.14)	28/347	0.92 (0.62, 1.36)	0.92 (0.58, 1.47)	47/347	1.03 (0.75, 1.41)	0.97 (0.66, 1.41)

>3	12/136	1.69 (0.93, 3.08)	1.30 (0.58, 2.89)	14/122	1.30 (0.74, 2.28)	1.38 (0.71, 2.66)	12/122	0.75 (0.41, 1.36)	0.63 (0.29, 1.36)
p for trend		0.81	0.73		0.66	0.59		0.53	0.35
Dark/black tea									
1-3	28/505	1.06 (0.72, 1.58)	0.98 (0.62, 1.55)	41/448	1.04 (0.75, 1.45)	1.20 (0.82, 1.76)	44/448	0.75 (0.54, 1.02)	0.82 (0.58, 1.16)
>3	9/182	0.95 (0.48, 1.86)	1.03 (0.49, 2.13)	16/156	1.17 (0.69, 1.96)	1.61 (0.92, 2.80)	19/156	0.92 (0.57, 1.50)	0.75 (0.41, 1.35)
p for trend		0.95	0.99		0.57	0.07		0.17	0.18

AGA: appropriate for gestational age; CI: confidence interval; SGA: small for gestational age; LGA: large for gestational age; OR: odds ratio.

*: Model adjusted for maternal age, educational level, monthly income, exposure to environmental tobacco smoke and folic intake during early pregnancy, pre-pregnancy BMI, previous history of complications during pregnancy, parity, sex of offspring, and where appropriate, frequency of other types of tea consumed.

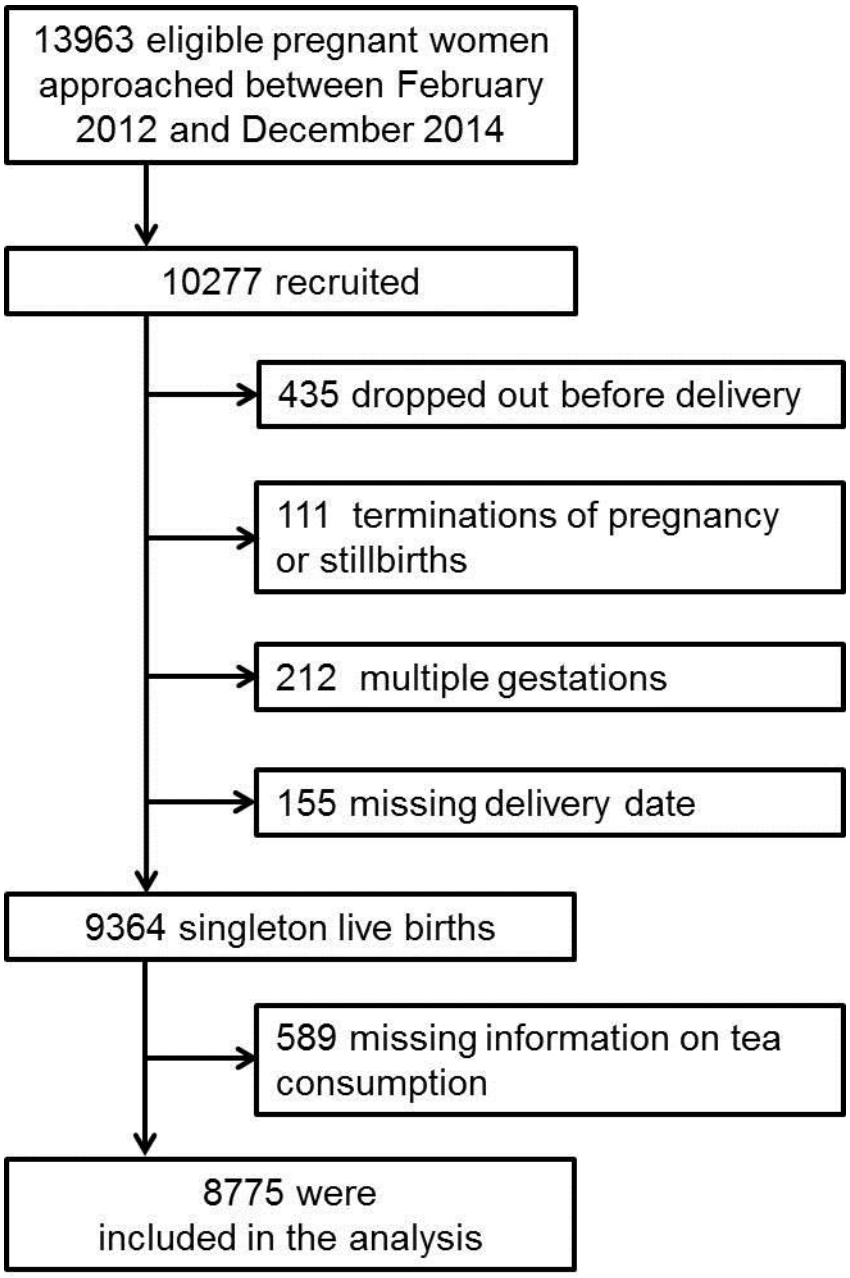
359 Table 3 Relationship between strength of tea and birth outcomes in the Born in Guangzhou Cohort Study, 2012-2014 (n=8775)

Strength of tea	Preterm birth			SGA			LGA		
	n	OR (95% CI)		n	OR (95% CI)		n	OR (95% CI)	
	(Preterm /term)	Crude	Adjusted *	(SGA /AGA)	Crude	Adjusted *	(LGA /AGA)	Crude	Adjusted *
Non-habitual drinkers (<1 serving/week)	364/6965	1.00 (Ref.)	1.00 (Ref.)	511/5659	1.00 (Ref.)	1.00 (Ref.)	760/5659	1.00 (Ref.)	1.00 (Ref.)
Green tea									
Weak	6/156	0.74 (0.32, 1.68)	0.89 (0.32, 2.50)	9/137	0.75 (0.38, 1.47)	0.89 (0.36, 2.17)	16/137	0.89 (0.53, 1.49)	0.76 (0.39, 1.49)
Moderate/strong	16/336	0.91 (0.55, 1.52)	0.89 (0.42, 1.90)	14/295	0.54 (0.31, 0.93)	0.53 (0.24, 1.13)	43/295	1.11 (0.80, 1.53)	1.02 (0.63, 1.63)
p for trend		0.58	0.77		0.02	0.10		0.67	0.91
Oolong tea									
Weak	5/204	0.47 (0.19, 1.15)	0.21 (0.06, 0.76)	17/170	1.14 (0.68, 1.88)	1.07 (0.53, 2.17)	22/170	0.98 (0.63, 1.54)	0.85 (0.44, 1.66)
Moderate/strong	19/340	1.07 (0.67, 1.72)	0.79 (0.40, 1.58)	25/296	0.96 (0.63, 1.46)	0.88 (0.49, 1.59)	37/296	0.95 (0.67, 1.34)	1.09 (0.66, 1.79)
p for trend		0.76	0.64		0.98	0.66		0.76	0.71

Dark/black tea									
Weak	14/313	0.86 (0.50, 1.48)	0.87 (0.43, 1.76)	23/272	0.96 (0.62, 1.48)	1.02 (0.58, 1.81)	32/272	0.89 (0.61, 1.30)	1.05 (0.61, 1.80)
Moderate/strong	22/372	1.13 (0.73, 1.76)	1.04 (0.57, 1.89)	34/329	1.17 (0.82, 1.69)	1.12 (0.69, 1.84)	31/329	0.72 (0.49, 1.04)	0.84 (0.51, 1.38)
p for trend		0.78	0.92		0.48	0.65		0.07	0.49

AGA: appropriate for gestational age; CI: confidence interval; SGA: small for gestational age; LGA: large for gestational age; OR: odds ratio.

*: Model adjusted for maternal age, educational level, monthly income, exposure to environmental tobacco smoke and folic intake during early pregnancy, pre-pregnancy BMI, previous history of complications during pregnancy, parity, sex of offspring, and total tea consumption frequency.


13963 eligible pregnant women approached between February 2012 and December 2014
10277 recruited
435 dropped out before delivery
111 terminations of pregnancy or stillbirths
212 multiple gestations
155 missing delivery date
9364 singleton live births
589 missing information on tea consumption
8775 were included in the analysis

365

366 Figure legends

367 Figure 1 Flowchart of participant recruitment in the Born in Guangzhou Cohort Study, 2012-

368 2014 (n=8775).