Coffee consumption and the risk of polycystic ovary syndrome: evidence from a case-control study

Yue Wang
Chongqing Medical University
Yin Yang
Chongqing Medical University
Hui Deng
Chongqing City Hospital of Traditional Chinese Medicine
Xiao-Qing Bu
Chongqing Medical University
Tian Li
The First Affiliated Hospital of Chongqing Medical University
Zhao-Hui Zhong (100144@cqmu.edu.cn)
Chongqing Medical University https://orcid.org/0000-0002-8057-3065
Xiao-Jun Tang
Chongqing Medical University
Qian Feng
Chongqing City Hospital of Traditional Chinese Medicine
Yu-Bin Ding
Chongqing Medical University
Li-Juan Fu
Chongqing Medical University

Research

Keywords: Polycystic ovary syndrome, Coffee consumption, Case-control study

Posted Date: September 20th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-889597/v1

Abstract

Background

Coffee has become one of the most common beverages worldwide. Some components in coffee have been reported to be beneficial to the regulation of hormones related to polycystic ovary syndrome(PCOS), and therefore may limit the development of PCOS. However, epidemiological evidence on the relationship between coffee consumption and PCOS is limited. In this study, we aimed at investigating the association between coffee consumption and PCOS risk.

Methods

The study was a hospital-based case-control study conducted at Chongqing Hospital of Traditional Chinese Medicine, China, from July 2018 to January 2020. Data was collected from 206 women with PCOS and 206 healthy women. A self-designed structured questionnaire was employed to collect relevant information from study participants. Sleep quality was evaluated by Pittsburgh Sleep Quality Index (PSQI). Logistic regression analysis was used to calculate odds ratios (ORs) and 95% confidence intervals (95% CI), adjusted for other confounding factors.

Results

A statistically significant inverse correlation was observed between coffee consumption and PCOS. After adjusting all potential confounding factors, the results of logistic regression analysis showed that compared to non-drinker, the ORs(95%CI) for ≤ 1 cup/week, 2–3 cups/week and > 3 cups/week were 0.322(0.180–0.574), 0.263(0.104–0.664) and 0.152(0.046–0.563), respectively, and the linear trend was also statistically significant(*P* for trend < 0.01).

Conclusions

Coffee consumption was found to be associated with a reduced risk of PCOS. Given the scarcity of studies on coffee consumption and PCOS, as well as the inherent limitations of our study, the prospective cohort studies in the future are needed to verify our results.

Introduction

Polycystic ovary syndrome (PCOS) is the most common reproductive endocrine disorder in women during reproductive ages and one of the main causes of female infertility and menstrual dysfunction. PCOS affects about 5–20% of women in reproductive age according to Rotterdam criteria(1). The clinical manifestation of PCOS is highly heterogeneous and mainly characterized by hyperandrogenism, ovarian dysfunction, and polycystic ovarian changes(2). However, the underlying etiology of the disease remains

not fully understood. At present, it is believed that PCOS may be the result of genetic and environmental factors, including dietary and lifestyle factors(3).

In addition to infertility and irregular menstruation, the majority of women with PCOS may also present with a series of metabolic abnormalities, including obesity, hyperandrogenism, dyslipidemia, insulin resistance/hyperinsulinemia, lower sex hormone-binding globulin (SHBG) levels, which are causal risk factors for PCOS and harmful to their long-term health(4–7). Among them, hyperandrogenism and insulin resistance, which are regarded as the primary endocrine characteristics of PCOS, have a critical role in the occurrence and development of PCOS(8). In addition, the SHBG level is known to decrease in patients with PCOS and is considered an indicator of hyperandrogenemia and abnormal metabolism(6). Due to these metabolic dysfunctions, these women also have an increased risk of developing type 2 diabetes, endometrial cancer, cardiovascular disease, and ovarian cancer(9–11).

Coffee has become one of the most common beverages worldwide. It contains more than 1000 components in addition to caffeine and is rich in many phytochemicals with various physiological effects(12). Some biological studies have shown that coffee consumption may be associated with PCOS due to the potential effect of caffeine or other components on hormonal regulation. Caffeine and chlorogenic acid in coffee, have been recognized to improve insulin sensitivity(13, 14). It was reported that increasing caffeine intake was inversely associated with bioavailable testosterone while positively correlated with SHBG(15, 16). From the point of view that coffee intake affects the regulation of hormones related to PCOS, there might also be a relation between coffee consumption and the risk of PCOS. However, there is still a lack of relevant epidemiological studies.

In this present study, we sought to investigate whether associations exist between coffee consumption and the risk of PCOS, independent of possible confounding factors, including sociodemographic characteristics, lifestyle factors, and other relevant variables.

Methods

We conducted a hospital-based case-control study to investigate PCOS-related risk factors in Chongqing from July 2018 and January 2020. All women with PCOS diagnosed for the first time by endocrine gynecology in Chongqing Hospital of Traditional Chinese Medicine were invited to participate in the study. As for the control group, healthy women with non-PCOS who underwent a physical examination at the hospital during the same period were included. Besides, due to the difficulty of collecting controls in the hospital, we also collected a small amount of data from healthy female graduate students in Chongqing Medical University as part of the control group.

Patients were diagnosed with PCOS if they have at least two of the following three characteristics according to the Rotterdam criteria(17):(1) Oligo- or anovulation; (2) clinical and/or biochemical hyperandrogenism, in which the primary clinical indicator is the presence of hirsutism; (3) Polycystic ovarian morphology (PCOM).

Patients were excluded from the study based on the presence of any of the following: congenital adrenal cortical hyperplasia, Cushing's syndrome, thyroid dysfunction, ovarian tumors or adrenal gland disorders that could ultimately cause ovulation disorders and abnormal androgen secretion, any other malignancy, current usage of any hormone therapy and pregnancy history in the past three months, lactation.

The research protocol was approved by the Ethics Committee of Chongqing Hospital of Traditional Chinese Medicine and all participants gave informed consent before participation in the study.

Data Collection

A structured questionnaire was administered and eligible participants completed the questionnaire. The questionnaire contained the following information: (1)sociodemographic characteristics, such as age, height, weight, monthly per-capita income, educational level, occupation type, ethnic group, residence area, marital status; (2) lifestyle of the individual including smoking and drinking habits, dietary habits; (3) sleep quality of the participants, assessed by the Pittsburgh Sleep Quality Index (PSQI) which included 19 items. Information on coffee consumption was obtained by a closed-ended question with four frequency categories: never, ≤ 1 cup/week, 2–3 cups/week and > 3cups/ week.

Statistical analysis

The IBM SPSS version 26.0 was employed for all statistical analyses. Shapiro-Wilk test was used to determine whether continuous data conform to normal distribution. All continuous variables following normal distribution were expressed as mean ± standard deviation, and categorical variables were presented as frequency and percentages. The Student's t-test and chi-square test were used to determine differences in sociodemographic variables between PCOS and control groups. Logistic regression analysis model was used to identify the association between coffee consumption and the risk of PCOS and to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) with the first category as the reference group. Models were adjusted for potential confounding factors, including age, BMI, marital status, other dietary habits, occupation type, night shift status, and PSQI total score. These variables are either clinically relevant or significantly associated with PCOS or suspected of affecting coffee consumption. A two-sided *P*-value of < 0.05 was considered to be statistically significant.

Results

Sociodemographic characteristics of the study subjects

A total of 206 PCOS cases and 206 controls were enrolled in the study. Table 1 shows the distribution of sociodemographic characteristics of the study subjects. Most of the participants in both groups were of Han ethnicity and lived in urban areas, with no significant difference between the two groups. There were also no significant differences in monthly income level, occupation

type and night shift status between PCOS cases and the control group. Compared with the control group, the mean age was significantly lower (30.09 vs 28.56, $P = 0.001$) and the mean BMI was higher (21.25 vs 22.53, $P < 0.001$) in PCOS cases. The majority of the study participants in both groups were married and the proportion of married women in the PCOS was significantly higher than that in the control group (82.5% vs 68.4%, $P < 0.001$). Additionally, a higher proportion of the control group was found with university or higher university degree in comparison to PCOS (62.1% vs 42.2%, $P < 0.001$). Further,

Table 1
Sociodemographic characteristics of the study subjects

Variables	PCOS(n = 206)	Control (n = 206)	*P*-value
Age	28.56(±3.95)	30.09(±4.98)	**0.001**
BMI	22.53(± 3.81)	21.25(± 2.81)	**< 0.001**
PSQI	6.34(±2.73)	5.64(±2.94)	**0.012**
Ethnicity			0.240
Han ethnicity	189(91.7)	195(94.7)	
Minority	24(8.3)	11(5.3)	
Residence			0.066
Urban	185(89.8)	195(94.7)	
Rural	21(9.2)	11(5.3)	
Education level			**< 0.001**
Secondary school or lower	12(5.8)	20(9.7)	
High school	107(51.9)	58(28.2)	
University/higher	87(42.2)	128(62.1)	
Income			0.065
< 5000 yuan	40(19.4)	28(13.6)	
5000 yuan~	89(43.2)	83(40.3)	
8000 yuan~	66(32.0)	89(43.2)	
missing	11(5.3)	6(2.9)	
Marital status			**< 0.001**
Single/divorced	36(17.5)	65(31.6)	
Married	170(82.5)	141(68.4)	
Occupation type			0.914

Data were presented as Mean(± SD) or No. (%).

PSQI: Total score of the Pittsburgh Sleep Quality Index.

Bold numbers signify those with statistical significance.

a significantly higher total score of PSQI was found in the PCOS group compared to controls (6.34 vs 5.64, $P = 0.012$).

Variables	PCOS(n = 206)	Control (n = 206)	*P*-value
Physical labor	28(13.6)	30(14.6)	
Mental labor	159(77.2)	159(77.2)	
missing	19(9.2)	17(8.3)	
Night shift			0.397
None	168(81.6)	171(83.0)	
< 3 times/month	17(8.3)	21(10.2)	
≥ 4 times/month	21(10.2)	14(6.8)	
Data were presented as Mean(± SD) or No. (%).			
PSQI: Total score of the Pittsburgh Sleep Quality Index.			
Bold numbers signify those with statistical significance.			
a significantly higher total score of PSQI was found in the PCOS group compared to controls (6.34 vs 5.64, *P* = 0.012).			

The results of univariate and multivariate analysis of factors related to PCOS

The univariate odds ratios and 95%CI of factors associated with PCOS are presented in Table 2. In this univariate logistic regression analysis model, PCOS was significantly associated with second-hand smoking, coffee consumption, dietary pattern and preference. Thus, these variables were included in the multivariate logistic regression model. The crude and adjusted association between coffee consumption and PCOS is shown in Table 3. In the unadjusted model, compared to non-drinkers, the OR(95% CI) for ≤ 1 cup/week, 2–3 cups/week and > 3 cups/week were 0.399(0.257–0.621), 0.305(0.145–0.643) and 0.170(0.061–0.474), respectively, *P* for trend < 0.001. In model 2, the OR(95% CI) for ≤ 1 cup/week, 2–3 cups/week and > 3 cups/week were 0.353(0.202–0.616), 0.314(0.128–0.770), 0.172(0.053–0.557), independent of age, BMI, education level, income, marital status, second-hand smoking, dietary pattern and preference. In model 3, after adjusting for all potential confounders, compared to non-drinkers, the OR(95%CI) for ≤ 1 cup/week, 2–3 cups/week and > 3 cups/week were 0.322(0.180–0.574), 0.263(0.104–0.664)

and 0.152(0.046–0.563), respectively. The linear trend was also statistically significant (*P* for trend < 0.001). The results indicated after gradual adjustment

for various relevant covariables, coffee consumption remained significantly associated with PCOS.

Table 2
Univariate logistic regression analysis for factors associated with PCOS.

Variables	Cases/controls	OR(95%CI)	*P*-value
Coffee intake			
No drinking	136/83	1(ref)	
≤ 1 cup/week	53/81	0.399(0.257–0.621)	**< 0.001**
2–3 cups/week	12/24	0.305(0.145–0.643)	**0.002**
> 3 cups/week	5/18	0.170(0.061–0.474)	**< 0.001**
Smoking			
Never/Past	193/197	1(ref)	
Current	13/9	1.193(0.456–3.122)	0.719
Second-hand smoking			
None	64/66	1(ref)	
1–3 days a week	39/79	0.509(0.304–0.852)	**0.01**
≥ 4 days a week	103/61	1.741(1.091–2.779)	**0.02**
Drinking habits			
Never/ever	106/102	1(ref)	
Current	100/104	0.925(0.629–1.362)	0.693
Mealtime			
Very regular	22/29	1(ref)	
Basically regular	135/157	1.133(0.622–2.065)	0.26
Not regular	49/20	3.230(1.51–6.905)	**0.002**
Three meals			
Very regular	125/154	1(ref)	
basically regular	27/25	1.331(0.735–2.407)	0.345
Not regular	54/27	2.467(1.467–4.139)	**0.001**
Gluttony			
Never/seldom	48/82	1(ref)	
Frequently	158/124	1.139(0.306–4.239)	0.846

Bold numbers signify those with statistical significance.

Variables	Cases/controls	OR(95%CI)	*P*-value
Midnight snack			
Never	37/41	1(ref)	
Seldom	147/138	1.180(0.715–1.949)	0.517
Frequently	22/27	0.903(0.441–1.850)	0.780
Snacks			
Never	7/11	1(ref)	
Seldom	129/131	1.547(0.582–4.116)	0.382
Frequently	70/64	1.719(0.628–4.702)	0.292
Dietary preference			
Balanced	96/129	1(ref)	
Partial to meat	50/38	1.768(1.075–2.908	**0.025**
Partial to vegetarian	60/39	2.067(1.277–3.348)	**0.003**
Bold numbers signify those with statistical significance.			

Table 3
Odds ratios and 95%CI for PCOS and coffee consumption from logistic regression models

Variables	Model 1	Model 2	Model 3
	OR(95%CI)	OR(95%CI)	OR(95%CI)
Coffee consumption			
Never	1	1	1
≤ 1 cup/week	0.399(0.257–0.621)	0.353(0.202–0.616)	0.322(0.180–0.574)
2–3 cups/week	0.305(0.145–0.643)	0.314(0.128–0.770)	0.263(0.104–0.664)
> 3 cups/week	0.170(0.061–0.474)	0.172(0.053–0.557)	0.152(0.046–0.563)
P for trend	**< 0.001**	**< 0.001**	**< 0.001**
Model 1: crude model(without adjustment).			

Model 2: adjusted for age, BMI, education level, income, marital status, second-hand smoking, dietary pattern and preference.

Model 3: adjusted for age, BMI, education level, income, marital status, second-hand smoking, dietary pattern and preference, occupation type, night shift, the total score of PSQI.

Bold numbers signify those with statistical significance.

Discussion

Our study provides epidemiological evidence on the inverse association between coffee consumption and PCOS in the Chinese population. The risk of PCOS had a decreasing trend with increased coffee consumption. Evidence from this dose-response relationship supports the biological reasonableness of our findings that higher coffee consumption may be a protective factor for PCOS.

So far, only a few studies have involved the relationship between coffee or caffeine intake and PCOS. In a randomized clinical trial involving 34 patients with PCOS investigating the effect of green coffee supplementation on androgen levels, supplementation of 400mg green coffee a day for 6 weeks was determined to be significantly associated with a reduction in free testosterone level, triglyceride, and cholesterol levels compared with the control group(18). Two case-control studies conducted in New York state and Spanish using food frequency questionnaire (FFQ) found that the caffeine intake of patients with PCOS was lower than that of the control group, but the difference was not statistically significant between PCOS and controls(19, 20). Nevertheless, these results should be interpreted with caution, as the authors of both studies mentioned that the sample size they included was relatively small, which may lead to a decline in the power to detect any association. Moreover, in addition to coffee, caffeine also exists naturally in tea leaves and is often added to other beverages as a food additive(21). It should be noted that coffee contains thousands of components, not just caffeine. Therefore, similar caffeine intake between the two groups did not indicate that there was no association between coffee and the risk of PCOS. Their results also provided the possibility that substances other than caffeine might play a vital role in the pathogenesis of PCOS. Further research is needed in the future to determine how coffee and its components affect PCOS.

Although it was previously believed that coffee should be consumed less or not at all for the possible adverse effects on human health, recent researches have shown that coffee may be beneficial because of its bioactive components(14, 22). Caffeine, along with chlorogenic acid(CGA), a mainly phenolic component in coffee, has been shown to be beneficial in maintaining metabolic homeostasis(23–25). Ma et al(26)studied the effect of CGA on obesity and insulin resistance in C57BL/6 mice. Obese mice were treated by 100 mg/kg CGA□intra-peritoneal□for 21 weeks. CGA suppressed diet-induced obesity and hyperinsulinemia, and improved insulin sensitivity when compared with the control group. Two prospective cohort studies found that not only caffeinated coffee but also decaffeinated coffee consumption was associated with body weight reduction(27, 28). A meta-analysis concluded that both caffeinated and decaffeinated coffee had protective effects against Type-2 diabetes and improved glucose metabolism(29). SHBG is a transport carrier protein that binds estrogen and androgen. Lower concentrations of SHBG are related to hyperandrogenism and insulin resistance, and affects long-term prognosis in PCOS patients (6, 30).Data from a large cohort study indicated that women who drank ≥ 4 cups of coffee a day had higher concentrations of SHBG(31). Taken together, our study and these studies

have shown that coffee could play a role in improving metabolic disorders and reducing the risk associated with PCOS.

However, there were some limitations in our study. First, due to the nature of case-control study, we could not determine a causal relationship between coffee consumption and PCOS. Secondly, since some of the control data were collected in the university, this could skew the distribution of educational levels towards one group. Although we have adjusted the educational level as a confounding factor in the multivariate logistic regression model, there may still be some deviations to some extent in our results. We recommend a more thorough and fair distribution of data in future studies. Moreover, the identification of coffee consumption was evaluated from a self-administered questionnaire, and not by a verified standardized questionnaire such as food frequency questionnaires, which may lead to some measurement errors due to the differences among people in the size of self-reported coffee cups. Additionally, we did not collect information about coffee types (caffeinated or decaffeinated), specific composition and content, which limited our preliminary exploration of whether caffeine or other substances in coffee play a critical role in the development of PCOS.

Conclusion

In conclusion, our study provided epidemiological evidence that higher coffee consumption reduces the risk of polycystic ovary syndrome. However, considering the scarcity of studies on coffee consumption and PCOS, as well as the inherent limitations of our study, more prospective cohort studies in the future are needed to verify our results.

Abbreviations

PCOS: polycystic ovary syndrome; SHBG:sex hormone-binding globulin.

Declarations

Acknowledgements

We would like to thank all the participants of this project and the medical staff or researchers who provided meaningful suggestions.

Authors' contributions

All authors read and approved the final manuscript.

Yin Yang: conception and the design of the study, data collection, funding acquisition. Yue Wang: analysis of data, drafting the manuscript. Hui Deng: data curation. Xiao-Qing Bu and Xiao-Jun Tang: methodology. Tian Li: investigation, resources. Qian Feng: funding acquisition. Yu-Bin Ding: supervision. Li-Juan Fu: project administration. Zhao-Hui Zhong: project administration, methodology.

Funding

This work was supported by funds from Natural Science Foundation of Chongqing (nos: cstc2019jcyj-msxmX0749,cstc2019jxjl130030,cstc2018jxjl130065) and Intelligent Medicine Research Project of Chongqing Medical University (NO.YJSZHYX202010).

Availability of data and materials

The datasets used and/or analyzed in the present study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Research approval was granted by the Ethics Committee of Chongqing Hospital of Traditional Chinese Medicine on 24/05/2018.

Consent for publication

All co-authors have seen and approved the final version of the paper and have agreed to its submission for publication.

Competing interests

The authors declare that they have no competing interests.

References

1. Lizneva D, Suturina L, Walker W, Brakta S, Gavrilova-Jordan L, Azziz R. Criteria, prevalence, and phenotypes of polycystic ovary syndrome. Fertil Steril. 2016;106(1):6–15.
2. Azziz R, Carmina E, Chen Z, Dunaif A, Laven JS, Legro RS, et al. Polycystic ovary syndrome. Nature reviews Disease primers. 2016;2:16057.
3. Escobar-Morreale HF. Polycystic ovary syndrome: definition, aetiology, diagnosis and treatment. Nature reviews Endocrinology. 2018;14(5):270–84.
4. Day FR, Hinds DA, Tung JY, Stolk L, Styrkarsdottir U, Saxena R, et al. Causal mechanisms and balancing selection inferred from genetic associations with polycystic ovary syndrome. Nat Commun. 2015;6:8464.
5. Macut D, Bjekić-Macut J, Rahelić D, Doknić M. Insulin and the polycystic ovary syndrome. Diabetes Res Clin Pract. 2017;130:163–70.
6. Zhu JL, Chen Z, Feng WJ, Long SL, Mo ZC. Sex hormone-binding globulin and polycystic ovary syndrome. Clin Chim Acta. 2019;499:142–8.
7. Stepto NK, Cassar S, Joham AE, Hutchison SK, Harrison CL, Goldstein RF, et al. Women with polycystic ovary syndrome have intrinsic insulin resistance on euglycaemic-hyperinsulaemic clamp.

Hum Reprod. 2013;28(3):777–84.

8. Wang J, Wu D, Guo H, Li M. Hyperandrogenemia and insulin resistance: The chief culprit of polycystic ovary syndrome. Life sciences. 2019;236:116940.
9. Norman RJ, Masters L, Milner CR, Wang JX, Davies MJ. Relative risk of conversion from normoglycaemia to impaired glucose tolerance or non-insulin dependent diabetes mellitus in polycystic ovarian syndrome. Hum Reprod. 2001;16(9):1995–8.
10. Ignatov A, Ortmann O. Endocrine Risk Factors of Endometrial Cancer: Polycystic Ovary Syndrome, Oral Contraceptives, Infertility, Tamoxifen. Cancers. 2020;12(7).
11. de Groot PC, Dekkers OM, Romijn JA, Dieben SW, Helmerhorst FM. PCOS, coronary heart disease, stroke and the influence of obesity: a systematic review and meta-analysis. Hum Reprod Update. 2011;17(4):495–500.
12. Cano-Marquina A, Tarín JJ, Cano A. The impact of coffee on health. Maturitas. 2013;75(1):7–21.
13. van Dam RM. Coffee and type 2 diabetes: from beans to beta-cells. #N/A. 2006;16(1):69–77.
14. Baspinar B, Eskici G, Ozcelik AO. How coffee affects metabolic syndrome and its components. Food Funct. 2017;8(6):2089–101.
15. Ferrini RL, Barrett-Connor E. Caffeine intake and endogenous sex steroid levels in postmenopausal women. The Rancho Bernardo Study. Am J Epidemiol. 1996;144(7):642–4.
16. Pihan-Le Bars F, Gusto G, Boutron-Ruault MC, Fagherazzi G, Bonnet F. Cross-sectional association of coffee and caffeine consumption with sex hormone-binding globulin in healthy nondiabetic women. Clin Endocrinol (Oxf). 2017;87(5):475–83.
17. Revised 2003 consensus. on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril. 2004;81(1):19–25.
18. Ahmad. Effect of green coffee supplementation on androgens level in women with polycystic ovary syndrome: A Randomized Clinical Trial. Obesity Medicine. 2020;20.
19. Lin AW, Kazemi M, Jarrett BY, Vanden Brink H, Hoeger KM, Spandorfer SD, et al. Dietary and Physical Activity Behaviors in Women with Polycystic Ovary Syndrome per the New International Evidence-Based Guideline. #N/A. 2019;11(11).
20. Álvarez-Blasco F, Luque-Ramírez M, Escobar-Morreale HF. Diet composition and physical activity in overweight and obese premenopausal women with or without polycystic ovary syndrome. Gynecol Endocrinol. 2011;27(12):978–81.
21. Reyes CM, Cornelis MC. Caffeine in the Diet: Country-Level Consumption and Guidelines. #N/A. 2018;10(11).
22. Gonzalez de Mejia E, Ramirez-Mares MV. Impact of caffeine and coffee on our health. Trends Endocrinol Metab. 2014;25(10):489–92.
23. Chen L, Teng H, Cao H. Chlorogenic acid and caffeic acid from Sonchus oleraceus Linn synergistically attenuate insulin resistance and modulate glucose uptake in HepG2 cells. Food Chem Toxicol. 2019;127:182–7.

24. Cornelis MC, Erlund I, Michelotti GA, Herder C, Westerhuis JA, Tuomilehto J. Metabolomic response to coffee consumption: application to a three-stage clinical trial. J Intern Med. 2018;283(6):544–57.
25. Bhandarkar NS, Mouatt P, Goncalves P, Thomas T, Brown L, Panchal SK. Modulation of gut microbiota by spent coffee grounds attenuates diet-induced metabolic syndrome in rats. FASEB J. 2020;34(3):4783–97.
26. Ma Y, Gao M, Liu D. Chlorogenic acid improves high fat diet-induced hepatic steatosis and insulin resistance in mice. Pharm Res. 2015;32(4):1200–9.
27. Lopez-Garcia E, van Dam RM, Rajpathak S, Willett WC, Manson JE, Hu FB. Changes in caffeine intake and long-term weight change in men and women. Am J Clin Nutr. 2006;83(3):674–80.
28. Greenberg JA, Axen KV, Schnoll R, Boozer CN. Coffee, tea and diabetes: the role of weight loss and caffeine. International journal of obesity (2005). 2005;29(9):1121-9.
29. Ding M, Bhupathiraju SN, Chen M, van Dam RM, Hu FB. Caffeinated and decaffeinated coffee consumption and risk of type 2 diabetes: a systematic review and a dose-response meta-analysis. Diabetes Care. 2014;37(2):569–86.
30. Thaler MA, Seifert-Klauss V, Luppa PB. The biomarker sex hormone-binding globulin - from established applications to emerging trends in clinical medicine. Best practice research Clinical endocrinology metabolism. 2015;29(5):749–60.
31. Hang D, Kværner AS, Ma W, Hu Y, Tabung FK, Nan H, et al. Coffee consumption and plasma biomarkers of metabolic and inflammatory pathways in US health professionals. Am J Clin Nutr. 2019;109(3):635–47.