

**Original Article****Increasing Consumption of Caffeinated Foods and Beverages Can Play Protective Roles against Cataract: A Case-control Study**Pedram Delgarm¹, Shirin Amini^{*2}, Younes Mohammadzadeh¹, Azam Jahangirimehr³, Mehdi Reza Ghomi⁴

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Received: March 2021

Accepted: June 2021

ABSTRACT

Background and Objectives: Cataract is the second cause of visual impairment and the first cause of blindness worldwide. This study was carried out to assess and compare quantities of caffeine consumption by cataract patients with healthy controls.

Materials and Methods: This case-control study was carried out on 336 40–80 year-old participants (168 patients with cataract and 168 healthy individuals). Demographic data, including age, gender, occupation, level of education, economic and marital statuses, levels of physical activity and history of smoking and chronic diseases, were collected using personal information questionnaire. Independent t-test and Mann-Whitney test were used to compare quantitative variables between the two groups. Chi-square test was used to compare categorical variables. Logistic regression was used to investigate relationships between the consumption of caffeinated foods and beverages and the odds ratios (OR) of cataract.

Results: Results showed that dietary consumption of caffeine played protective roles against occurrence of cataracts [OR: 0.982 (CI: 0.977, 0.988), p -value < 0.001]. Exposure to ultraviolet light of the sun was also a significant factor in increasing risks of cataract [OR: 2.32 (CI: 1.29, 4.19), p -value = 0.005].

Conclusions: Increasing consumption of caffeinated foods and beverages can play protective roles against cataract.

Keywords: Cataract, Caffeinated foods, Protection, Iran

Introduction

Cataract is a multifactorial disease caused by genetic, environmental and metabolic factors. Cataract leads to mutations in the expression of crystalline gene in lens of the eyes. Changes in this gene turn its products into water-insoluble ones. This results in accumulation of altered and insoluble crystals in water, which leads to opacity of the lens of eyes and decreased visual acuity (1). Symptoms of the disease usually include blurred vision, scattering of stars such as light around, changes in colors of objects that are usually seen in red or yellow, glare, altered contrast sensitivity, myopia and squint or multiple noses (1, 2). According to the World Health Organization (WHO), cataract is the cause of blindness in 27–45 million people (3) and the second cause of visual impairment worldwide (4, 5). In Iran, the disease is responsible for 50–90% of blindness cases (5). Prevalence of cataract in people aged 40–49 years in Tehran is 1.9% and in people over 50 year-

old is 17.1% (3). Caffeine is a crystalline, white and bitter-tasting substance, known as 1,3,7-trimethylxanthine with the formula of $O_2N_4C_8H_{10}$ and stimulant alkaloids. The chemical is found in coffee, tea, chocolate and beverages (6, 7). Caffeine includes antioxidant characteristics and may prevent oxidative damages to lens of the eye as an inhibitory agent (8–14). Coffee includes high quantities of caffeine and special antioxidants such as chlorogenic acid, which may help decrease risks of cataract. Studies have shown that nutrients with antioxidant characteristics such as vitamins C and E and caffeine include significant effects on preventing cataract [15–18]. Results of a case-control study in mice have shown that caffeine plays roles in preventing cataract by inhibiting oxidative stress in normal lens metabolism (18, 19). Studies have also investigated roles of caffeine in improving lens health; as investigated by the current study (22–25).

In fact, caffeine is a relatively-cheap nutrition while cataract treatment is expensive. Up-to-date, human studies in this field are limited. Therefore, the present study was carried out to investigate relationships between the history of consumption of caffeinated foods and beverages and the occurrence of cataract in 40–80 year-old patients from Shoushtar, Iran.

Materials and Methods

This case-control study was carried out on 336 40–80 year-old participants (168 patients with cataract and 168 healthy individuals). After approval of the study in Ethics Committee of Shoushtar Faculty of Medical Sciences and receiving consents from the eligible participants, participants were enrolled in the study. Furthermore, protocol of the study was verified by the Medical Ethics Committee, Shoushtar Faculty of Medical Science, based on 2013 Helsinki Declaration (registration no. IR.SHOUSHTAR.REC.1399.027). Patients with cataract were selected within those referred to the Eye Clinic or admitted to the Ophthalmology Ward of Khatam Al-Anbia Hospital, Shoushtar, Khozestan Province, Iran. Control group was selected from 40–80 year-old people with no cataracts, referred to the Output Clinic of Khatam al-Anbia Hospital. Case and control groups were assessed to be similar in terms of age and gender. Having willingness to cooperate, being man or woman between the ages of 40 and 80 years, and diagnosed and approved with cataracts by a physician in the last 2–3 months (case group) were the inclusion criteria. Being under the age of 40 and over the age of 80 years, having history of infections with glaucoma and increased eye pressure, having galactosomal involvement, having unwillingness to cooperate, receiving drugs that affect eyes, being hospitalized due to cardiovascular diseases (CVD), cancers and kidney, endocrine, nervous system, skin, bone and gastrointestinal tract (GIT) diseases with adverse effects on the eye health were the exclusion criteria.

Demographic data, including age, gender, occupation, education, economic and marital statuses, physical activity and history of smoking and chronic diseases, were collected using personal information questionnaires. Height was measured using gauge with an accuracy of 0.1 cm and weight was measured using digital scale with an accuracy of 0.5 kg. Moreover, waist measurements were carried out by the researchers using inelastic meter with an accuracy of 0.1 cm. Levels of education and income were asked from the participants and categorized. Participants with an income of less than 40 million Rials were considered as low-income, participants with an income of 40–70 million Rials were considered as middle-income and those with an income of more than 70 million Rials were considered as good income participants. Education was categorized to elementary, diploma and college educations. Quantity of

the caffeine consumption was assessed during the last year in the healthy group and during the year before diagnosis of the disease in the case group using Food Frequency Questionnaire (FFQ). Moreover, FFQ designed and validated for the Iranian population (20) was used and volume size and frequency of the consumption of all foods, especially caffeinated foods (cereals, dairy, meats, fruits and vegetables) and beverages, in the last year were asked. Then, energy, macronutrient and caffeine intakes were calculated using Nutrient 4 Software. Moreover, FFQ designed and validated for the Iranian population (21) was used and foods consumption by the participants during the last year were asked. Then, energy intake was calculated using Nutrient 4 Software. Short-form of the international physical activity questionnaire (IPAQ) was used to investigate physical activity levels. The total metabolic equivalent (METs) was calculated based on the usual physical activity of the participants. Then, participants were classified into three major groups based on their levels of activity, including 1) low, 2) medium and 3) high groups. Reliability and validity of IPAQ were verified in a previous study in Iran (22). Weekly number and duration time of exposure to sunlight within the last three years were asked from the participants as well. Due to the lack of appropriate studies on the consumption of caffeine and its association with cataract, the sample size was calculated based on the previous studies (16). Considering the ratio of vitamin E consumption in the cataract group ($p_1 = 22\%$) compared to the control group ($p_2 = 38\%$) and $\alpha = 0.05$ (type I error) and $\beta = 0.1$ (type II error), the sample size for each group was calculated as 168 (total sample size of 336).

Statistical analysis

Independent t-test and Mann-Whitney test were used to compare quantitative variables between the two groups based on the normality of data distribution. Chi-square test was used to compare categorical variables between the case and control groups. Logistic regression was used to investigate relationships between the consumption of caffeinated foods and beverages and the odds ratios (OR) of cataract. Associations were assessed in crud OR and then BMI, energy intake, physical activity and age were included in Model 1. Statistical analysis was carried out using SPSS Software v.19 (SPSS, Chicago, IL, USA).

Results

The mean age of the participants was 59.30 ± 10.77 . The mean BMI of the participants was 26.58 ± 4.93 and their mean waist circumference was 93.05 ± 15.33 . Furthermore, BMI and waist circumference in the cataract group were significantly higher than those in the healthy group ($p = 0.001$ and $p = 0.001$, respectively). Patients with cataract included significantly lower levels of physical activity, primary education and total income ($p < 0.001$,

$p < 0.001$, $p < 0.001$, respectively). Dietary intakes of the two groups are shown in Table 2. The average calorie intake of the participants was $2493.71 \text{ cal.} \pm 517.32$. Consumption of caffeinated foods in the healthy group was higher than that in the case group ($p < 0.001$). Intake of protein in the case group was significantly lower than that in the other group ($p = 0.018$). No statistically significant differences were seen

in the intakes of energy, water, carbohydrates, fibers and fats between the healthy and the case groups. Results of Table 3 showed that dietary intake of caffeine included protective roles against cataract. Exposure to ultraviolet (UV) light of the sun was a significant factor in increasing risks of cataract.

Table 1. Comparison of basic characteristics and anthropometric measures of the participants

Characteristic	Case (Cataract) N=168	Control (Healthy) N=168	P-Value
Age†	57.05±7.73	55.55±12.02	0.051
Sex n (%) ‡			0.06
Female	77(45.8)	100(59.5)	
Male	91(54.2)	68(40.5)	
Weight (kg)†	73.28±11.421	72.95±12.047	0.79
Height (cm)†	160.25±23.66	167.02±9.08	0.001**
Waist circumference (cm)†	99.35±15.508	86.76±20.735	0.001**
BMI (kg/m ²)†	27.78±4.93	26.19±3.95	0.001**
Physical activity levels n (%)‡			<0.001**
Low	88(52.4)	48(28.6)	
Medium	75(44.6)	101(60.1)	
High	5(3.0)	17(10.1)	
Educational level n (%) ‡			<0.001**
Elementary	108(64.3)	46(27.4)	
Diploma	54(32.1)	68(40.5)	
College	6(3.6)	52(31.0)	
Smoking history n (%)‡			0.36
No	145(86.3)	139(82.7)	
Tobacco	2(1.2)	5(3.0)	
cigarettes	20(11.9)	20(11.9)	
Tobacco and cigarettes	1(0.6)	4(2.4)	
Financial situation (n, %) ‡			<0.001**
Lower-middle	73(43.5)	30(17.9)	
Middle	89(53.0)	106(63.1)	
Upper-middle	6(3.6)	31(18.5)	

† Data are expressed as mean (standard deviation) and analyzed by independent sample t test.

‡ Data are expressed as n (%) and analyzed by chi-squared test.

Data are expressed as n (%) and analyzed by Fisher exact test.

BMI, body mass index; P-value <0.05 was considered significant. * $p < 0.05$, ** $p < 0.01$

Table 2. Comparison of dietary intakes of caffeine and macronutrients by the participants

Nutrient	Control (Healthy) N=168	Case (Cataract) N=168	p-value
Energy (kcal) †	2503.60±464.08	2490.82±548.99	0.12
Caffeine (mg) †	125.32±65.30	74.57±38.42	<0.001**
Water (glass/day) ‡	5.27(2.11, 6.01)	5.08(3.10, 6.92)	0.302
Carbohydrate (g) †	361.51±78.83	336.34±76.68	0.077
Fiber(g) †	58.97±22.62	59.70±19.50	0.10
Protein (g) †	101.39±19.38	93.72±21.96	0.018*
Fat (g) †	92.97±26.41	85.99±27.41	0.070

† Data are expressed as mean (standard deviation) and analyzed by independent sample t test.

P-value <0.05 was considered significant. * $p < 0.05$, ** $p < 0.01$

Table 3. Occurrence of cataract with intakes of caffeine and macronutrients using odds ratios (OR) and 95% confidence intervals (CI)

Nutrient intake	Crude OR	P-value	Adjusted OR Model 1	P-value
Exposure to UVB	1.92(1.12, 3.30)	0.017*	2.31(1.28, 4.02)	0.004**
Caffeine (mg)	0.983(0.977, 0.988)	<0.001**	0.981(0.975, 0.978)	<0.001**
Water	0.931(0.812, 1.06)	0.31	0.966(0.812, 1.13)	0.634
Carbohydrate (g)	0.997(0.994, 1.00)	0.8	0.990(0.991, 0.998)	0.24
Fiber(g)	1.02(0.02, 1.04)	<0.14	1.04(0.01, 1.040)	0.50
Fat (g)	0.993(0.98, 1.00)	0.09	0.990(0.981, 1.00)	0.08
Protein (g)	0.990(0.95, 1.01)	0.07	0.992(0.94, 1.05)	0.06

OR calculated by *logistic regression*. BMI and waist circumference was included in the model 1. *P*-value <0.05 was considered significant.

p* < 0.05, *p* < 0.01

Discussion

Cataract is described as a public health problem worldwide. Several factors play roles in the pathogenesis of this disease, investigated in the present study. Based on the results, the case group included higher levels of BMI and waist circumference as well as lower levels of physical activity, education and income. Case-control study was carried out with the major purpose of assessing possible relationships between the consumption of caffeinated foods and beverages and the occurrence of cataract. Studies have shown that consumption of coffee can increase nitric oxide (NO), tumor necrosis factor alpha (TNF- α), interleukin 9 beta (IL-9 β), malondialdehyde and calcium pump that leads to increased calcium in cells, stimulated oxidation and production of reactive oxygen species (ROS) and decreased superoxide dismutase (SOD) in the lenses. In addition, caffeine maintains concentration of glutathione in the lens and helps prevent oxidative stress and maintain metabolic function and tissue transport. These changes play roles in preventing oxidative stress in the lens cells. Therefore, coffee can be effective in preventing and improving conditions of cataracts. Results showed that increased exposure to the sunlight could increase the occurrence of cataracts. In contrast, increased consumption of caffeinated foods and beverages played protective roles against cataract.

In an ecological study on the prevalence of cataract-induced blindness in combination with other eye diseases such as glaucoma, diabetic retinopathy, trachoma and age-related degenerative macular degeneration, results showed that caffeine was involved in inhibiting formation of ROS and thus preventing cell damages. They showed that groups that received further coffee included lower chances of developing cataract; as shown by the present study (17). Results of another case-control study in mice demonstrated that caffeine played roles in preventing cataract by maintaining adenosine triphosphate (ATP) levels by inhibiting oxidative stress and maintaining normal lens metabolism and regenerative glutathione levels (18). Caffeine showed preventive roles against oxidative stress

by maintaining glutathione concentrations in lenses and thus maintaining metabolic function and tissue transport as well as preventing induction of apoptosis (19). In a study, lens of the eyes was examined to analyze the quantity of caffeine and its pharmacokinetic effects on health of the lens after coffee consumption by the patients with cataract. Caffeine could include preventive effects on cataract after absorption (8). In another study, effects of caffeine on the prevention of ascorbic acid and glutathione depletion due to high-fat diets were investigated. Results showed that coffee consumption prevented decreases of ascorbic acid caused by high-fat diets in the lenses. In general, caffeine could prevent decreases in ascorbic acid and glutathione in the lens and the level of ascorbic acid depended on the level of caffeine (23). Moreover, studies investigated roles of caffeine in improving lens health and results were similar to those from the present study (24–26).

Naturally, microribonucleic acids (miRNAs) play significant roles in cell death, proliferation and stress response. Oxidative stress can activate miRNAs through the production of ROS, leading to the destruction of ocular lens tissue cells. Caffeine consumption inhibited these miRNAs. Therefore, protective effects of caffeine against cataract were attributed to the ability of this compound to prevent the formation of proapoptotic miRNAs (27). One of the limitations in this study was the use of specific community and region with similar eating habits and cultures. This has led to limitations in comparing various food consumptions between the individuals. Due to the use of a specialized ophthalmology clinic in the area because of high number of visits and limited access to individuals, access to comprehensive information was limited. However, the current findings can provide basic information in other areas in terms of relative educational level, economical status and average caffeine consumption.

Conclusion

Increased exposure to the sunlight can increase the occurrence of cataract. Increasing consumption of

caffeinated foods and beverages can play protective roles against cataract.

Acknowledgement

This study was financially supported by the Vice-Chancellor for Research Affairs of Shoushtar Faculty of Medical Sciences, Shoushtar, Iran (grant no. 98000036).

Financial disclosure

The authors declare no conflict of interests.

Ethical Approval: The Medical Ethics Committee of Shoushtar Faculty of Medical Sciences approved the study protocol based on the guidelines of 2013 Helsinki Declaration (registration no. IR.SHOUSHTAR.REC.1399.027). All participants signed consent forms.

Consent to Participate: Written informed consents were received from the participants

Authors' contributions: P.D and S.A contributed in the conception and design, analysis of data and interpretation of the study as well as writing and revision of the manuscript. A.J, Y.M and M.R.G contributed to the critical revision of the manuscript. All authors approved the final version of the manuscript before submitting.

References

1. Kumary RP, Ramkumar S, Thankappan B, Anbarasa K. Etiology and prevention of cataract. *Studies on the cornea and lens*.2015; 287-315.
2. Shabanynejad A, Zargarani A, Mehdizadeh A, Khalili M. Cataracts in the texts of Iranian traditional medicine (Mansouri's law in medicine and ferdows al-hikma). *Bina*.2012;18(3):344-348.
3. Sahebalzamani M, Kosha S, Heidary M, Safavy M, Farshid P, Esmaeely I. Investigating the predisposing factors of age-related cataracts in clients of ophthalmology centers affiliated to Tehran university of medical sciences. *Islamic Azad University, Tehran Medical Branch*.2009;20(4):273-277.
4. Hashemy H, Rezvan F, Fotohy A, Gilasy H, Asgary S, Papey O, et al. Cataract surgery in khorasan razavi province during the 2006 to 2011. *Journal of Mashhad Paramedical and Rehabilitation Sciences*.2013;3(1):7-15.
5. Mobashery M, Barony M, Alidosty M, Yosefy M, Memarzadeh A, Behzady Y. Comparison of quality of life of patients over 50 years before and after cataract surgery in chaharmahal and bakhtiari province. *Journal of Iran University of Medical Sciences*.2012;21(6):73-167.
6. Foraty H, Hojjaty Z, Rahmaninia F. The effect of acute caffeine consumption on muscle strength and endurance of amateur male soccer players. *Applied Biological Sciences in Sports*.2013;2(4):68-77.
7. Ranjbar R, Kordy M, Gaeni A. The effect of caffeine consumption on anaerobic power, fatigue index and blood lactate levels of male students athletes. *Journal of Sports Biological Sciences*.2008;1(1):123-136.
8. Kronschräger M, Stimpfl T, Rieß M, Hirschschall N, Leisser C, Findl O. Pharmacokinetics of Caffeine in the Lens Capsule/Epithelium After Peroral Intake: A Pilot Randomized Controlled Study. *Investigative ophthalmology & visual science*. 2018;59(5):1855-60.
9. Kronschräger M, Löfgren S, Yu Z, Talebizadeh N, Varma SD, Söderberg P. Caffeine eye drops protect against UV-B cataract. *Experimental eye research*. 2013;113:26-31.
10. Varma SD, Kovtun S. Protective effect of caffeine against high sugar-induced transcription of microRNAs and consequent gene silencing: a study using lenses of galactosemic mice. *Molecular vision*. 2013;19:493.
11. Varma S, Hegde K, Kovtun S. Oxidative stress in lens in vivo: inhibitory effect of caffeine. A preliminary report. *Molecular Vision*. 2010;16:501.
12. Varma SD, Hegde KR. Prevention of oxidative damage to lens by caffeine. *Journal of Ocular Pharmacology and Therapeutics*. 2010;26(1):73-8.
13. Varma SD, Hegde KR, Kovtun S. UV-B-induced damage to the lens in vitro: prevention by caffeine. *Journal of Ocular Pharmacology and Therapeutics*. 2008;24(5):439-44.
14. Varma SD, Kovtun S, Hegde KR. UV-Induced Apoptosis in Lens: Prevention by Caffeine. *Journal of Caffeine Research*. 2011;1(2):131-6.
15. Rautiainen S, Lindblad BE, Morgenstern R, Wolk A. Total antioxidant capacity of the diet and risk of age-related cataract: a population-based prospective cohort of women. *JAMA ophthalmology*. 2014;132(3):247-52.
16. Robertson JM, Donner AP, Trevithick JR. Vitamin E Intake and Risk of Cataracts in Humans a. *Annals of the New York Academy of Sciences*. 1989;570(1):372-82.
17. Varma SD. Effect of coffee (caffeine) against human cataract blindness. *Clinical ophthalmology (Auckland, NZ)*. 2016;10:213.
18. Varma SD, Hegde KR, Kovtun S. Inhibition of selenite-induced cataract by caffeine. *Acta ophthalmologica*. 2010;88(7):245-9.
19. Varma SD, Kovtun S, Hegde K. Effectiveness of topical caffeine in cataract prevention: studies with galactose cataract. *Molecular vision*. 2010;16:2626.
20. Mirmiran P, Esfahani FH, Mehrabi Y, Hedayati M, Azizi F. Reliability and relative validity of an FFQ for nutrients in the Tehran lipid and glucose study. *Public Health Nutr*. 2010;13:654-62.
- 21-Mohseni H, Malek Mohammadi F, Karampour Z, Amini S, Abiri B, Sayyah M. The relationship between history of dietary nutrients intakes and incidence of aggressive behavior in adolescent girls: A case-control study. *Clin Nutr ESPEN*. 2021;43:200-205.
- 22-Vasheghani-Farahani A, Tahmasbi M, Asheri H, Ashraf H, Nedjat S, Kordi R. The Persian, last 7-day, long form of the International Physical Activity Questionnaire: translation and validation study. *Asian J Sports Med*. 2011; 2:106.
23. Nakazawa Y, Ishimori N, Oguchi J, Nagai N, Kimura M, Funakoshi Tago M, et al. Coffee brew intake can prevent the reduction of lens glutathione and ascorbic acid levels in HFD fed animals. *Experimental and therapeutic medicine*. 2019;17(2):1420-5.
24. Taalat MS, Aly EM, Mohamed ES, Ali MA, Gaber HA. Caffeine and nifedipine effect on cataract induced by

- selenite in rats. *Journal of The Arab Society for Medical Research*. 2018;13(1):32.
25. Yu X, Zheng H, Chan MT, Wu WKK. MicroRNAs: new players in cataract. *American journal of translational research*. 2017;9(9):3896.
26. Ishimori N, Oguchi J, Nakazawa Y, Kobata K, Funakoshi-Tago M, Tamura H. Roasting enhances the anti-cataract effect of coffee beans: Ameliorating selenite-induced cataracts in rats. *Current eye research*. 2017;42(6):864-70.
27. El Okda E, Mohamed M, Shaheed E, Abdel-Moemin A. Switching to instant black coffee modulates sodium selenite-induced cataract in rats. *GMS German Medical Science*. 2016;14.