

Prevalence of carotid artery calcification detected by digital panoramic radiographs in a sample of yemeni dental patients.

Prevalencia de la calcificación de la arteria carótida detectada por radiografías panorámicas digitales en una muestra de pacientes dentales yemeníes.

Jameel Helmi.¹ Zakria Alhariri.¹ Khaled AL-Jawfi.¹ Anas Shamala.¹

Affiliations: ¹Departament of Biological & Preventive Sciences, College of Dentistry, University of Science & Technology, Yemen.

Corresponding author: Anas Shamala. University of Science & Technology, Sanaa Yemen. Email: anasshamala@gmail.com

 Receipt:
 02/14/2019
 Revised:
 04/23/2019

 Acceptance:
 05/31/2019
 Online:
 12/30/2019

Cite as:

Helmi J, Zakria Alhariri Z, AL-Jawfi K & Shamala A. Prevalence of carotid artery calcification detected by digital panoramic radiographs in a sample of yemeni dental patients.

J Oral Res 8(6):510-516. Doi:10.17126/joralres.2019.076

Abstract: Background: Carotid artery calcification (CAC) is one of risk factors of cardiovascular disorders (CVDs). Digital panoramic radiographs can detect it. Aim of the study: This study aimed to determine the prevalence of CAC detected by digital panoramic radiographs in a sample of Yemeni dental patients. Materials and Methods: An observational and analytical cross-sectional study was used to investigate a convenience sample of 443 patients. These patients were interviewed face-to-face for their socio-demographic information and their medical background regarding CVDs and associated risk factors. The researchers for detection of CAC assessed the digital panoramic radiographs. Results: High income and middle-aged patients were risk factors of CVDs significantly associated with increased incidence of CAC (42 patients (9.5%) and 32 patients (7.2%), respectively). Patients with a previous medical consultation, previous medications and family history of CVDs revealed a significant higher prevalence of CAC (p=0.001). Conclusion: There was an increased prevalence of CAC detected on digital panoramic radiographs, as a risk factor of CVDs. CAC was more common in females than males.

Keywords: Prevalence; carotid artery diseases; cardiovascular diseases; carotid arteries; calcinosis; radiography, panoramic.

Resumen: Antecedentes: La calcificación de la arteria carótida (CAC) es uno de los factores de riesgo de enfermedades cardiovasculares (ECV). La CAC puede ser detectada por radiografías panorámicas digitales. Objetivo del estudio: Este estudio tuvo como objetivo determinar la prevalencia de CAC detectada por radiografías panorámicas digitales en una muestra de pacientes dentales yemeníes. Materiales y métodos: Se utilizó un estudio transversal observacional y analítico para investigar una muestra de conveniencia de 443 pacientes. Estos pacientes fueron entrevistados en persona para obtener su información sociodemográfica y sus antecedentes médicos con respecto a las ECV y los factores de riesgo asociados. Los investigadores evaluaron las radiografías panorámicas digitales para detectar CAC.Resultados: Los pacientes de ingresos altos y de mediana edad fueron factores de riesgo de ECV significativamente asociados con una mayor incidencia de CAC (42 pacientes (9,5%) y 32 pacientes (7,2%), respectivamente). Los pacientes con una consulta médica previa, medicamentos previos y antecedentes familiares de ECV revelaron una prevalencia significativamente mayor de CAC (p=0.001). Conclusión: Hubo una mayor prevalencia de CAC detectada en radiografías panorámicas digitales como factor de riesgo de ECV, y CAC fue más común en mujeres que en hombres.

Palabras Clave: Prevalencia; enfermedades de las arterias carótidas; enfermedades cardiovasculares; arterias carótidas; calcinosis; radiografía panorámica.

INTRODUCTION.

Cardiovascular disorders (CVDs) are responsible for substantial morbidity, mortality, and financial costs. The most common risk factors for CVDs are obesity, type II diabetes, arterial hypertension, smoking, and lifestyle.¹ Arterial stenosis as a result of an atheroma at the carotid artery bifurcation is the most frequent risk factor for cerebrovascular accidents.²

On other hand, nowadays the use of digital panoramic radiography (DPR) of the jaw has been indicated as a noninvasive, reliable and low-cost diagnostic technique to detect carotid artery calcification (CAC) or plaque, through the appearance of a heterogeneous and nodular radiopaque mass, situated above, below or within the C^{3-4} intervertebral disc space at an angle of 45° from the mandibular angle according to the hyoid bone and the epiglottis.

In general, atherosclerosis affects the medium and large arteries through the formation of calcification of arteries walls, and there are several factors that increase the incidence of this atherosclerosis, including blood pressure, age, gender, diabetes, obesity, smoking and family history.⁴ In 2014, Moshfeghi et al. reported on the association between CAC found through DPR and two cerebrovascular accident risk factors: hypertension and myocardial infarction. The association found was significant.

Therefore, it seems that the CAC identified on panoramic images of dental patients should be detected by dentists. However, Atalay *et al.*,⁵ conducted a rigorous scientific research that aimed to evaluate the incidence of CAC from DPR and concluded that some patients had CAC and had to be referred to specialized healthcare professionals.⁶ Borba *et al.*,⁷ reported that the importance of the DPR and its credibility in detecting the existence of sclerosis, and found that DPR is significantly accurate and effective and it expedites the appropriate medical intervention for patients who are doubtful, in order to reduce the cost for the patient and morbidity within the community.

However, in 2017, Friedlander *et al.*,³ conducted a descriptive retrospective study that concluded that CAC often heralds an ischemic stroke and may be seen on DPR of patients with gout, especially those of increased

age, with dyslipidemias or diabetes.

Thus, dentists must be uniquely vigilant in detecting these lesions when evaluating the images of all patients with gout, especially those with additional risk factors.⁸ More recently, Nasseh *et al.*,⁹ concluded that CAC can be found on routine DPR at dental clinics. Dentists should automatically refer the patients in question for specialized medical evaluation. DPR may have some diagnostic importance for detecting CAC closely connected to atherosclerosis, thus preventing major life-threatening events such as cerebrovascular accidents.

There are no studies in Yemen aimed to find the relationship between diagnostic CAC from DPR and CVDs risk factors. Therefore, the present study aimed to determine the prevalence of CAC detected by DPR with CVD risk factors among dental clinic patients in Sana'a city, Yemen.

MATERIALS AND METHODS. Study design

An observational and analytical cross-sectional study. Study sample

The study was conducted on 443 patients referred from several dental clinics in Sana'a city to the unit of Digital Panoramic Radiography from November 2017 to February 2018 at the College of Dentistry, University of Science and Technology, Yemen.

Exclusion Criteria

All patients referred for DPR were included except patients under the age of 15 years old, referred for DPR as an emergency case, patients with upper GI tract infections or any type of cancers, patients who refused to participate in the study, patients with psychological disorders, and pregnant women.

Data Collection

The data were collected by using several tools included Digital Panoramic X-Ray Machine (Vatech PaX-I-2500, Korea), Weight Measuring Device (SECA, Australia), Length Measuring Device accredited by UNICEF and the Yemeni Ministry of Public Health and Population (Stature, China), the body mass index was calculated, and a structured questionnaire was used to interview patients, and which included four parts: -Socio-demographic characteristics of the patients (sex, age, body mass index, marital status, occupation, level of education, place of residency, and income).

- Lifestyle (smoking, coffee and tea consumption, soda consumption, khat chewing, fast food consumption, and regular physical activity).

-Medical history of patients with CVD and associated risk factors which includes central chest pain, history of medications and herbals for CVD, history of heart attacks or strokes, hypertension, diabetes, high cholesterol, obesity, family history of atherosclerosis and/or strokes.

- Results from DPR.

Radiographic examinations of CACs

DPR of the patients were all taken by the same radiologist. The DPRs were examined for the presence of CAC. The CAC radiation tests were done by a digital sensor system with two dimension examinations. Moreo-ver, each patient with positive CAC was informed and referred to cardiologists for consultation and further management.

A pilot study

A pilot study was carried out on 45 participants representing 10% of the estimated sample size and its results were analyzed by Chronbach's Alfa to test the reliability of the pilot study. The reliability scored 82.8%.

Ethics approval and informed consent from patients

Prior to the study, ethics approval to carry out this study was granted from the ethics committee of the Faculty of Medicine and Health Sciences, University of Science & Technology (MECA No. 2017/15). The study was explained to all patients and informed consents were anonymously obtained from each patient to confirm their enrollment in the study.

Sample size

The minimal sample size was 211 patients calculated using the OpenEpi software (MIT, USA). The total number of patients who attended to the Department for DPRs were 517, 74 patients were excluded, so the final sample size was 443 patients; sampling was done by convenience.

Data Analysis

Data were collected, recorded, revised, arranged, coded and entered into SPSS software (version 22) for analysis. The results were tabulated and figures were constructed. Chi-Square test was used with significance set at p < 0.05.

	Variable	Normal DPR*		Abnormal DPR (CAC**)			
		n	%	n	%	<i>p</i> -value	
Age by years:	15 – 40	155	34.9	18	4.1	0.001***	
Mean (\pm SD) = 46.0(\pm 17.6)	41 – 65	169	38.2	32	7.2		
	> 65	50	11.3	19	4.3		
Gender	Male	175	39.5	20	4.5	0.933	
	Female	199	44.9	49	11.1		
Obesity:	Yes	104	23.5	20	4.5	0.727	
Mean (±SD) = 27.7 (±7.4)	No	270	60.9	49	11.1		
Level of Education	Primary Education or less	67	15.1	12	2.7	0.092	
	Secondary Education or more	307	69.3	57	12.9		
Income	Insufficient	117	26.4	15	3.4	0.027***	
	Accepted	215	48.5	42	9.5		
	Sufficient	42	9.5	12	2.7		

 Table 1. Distribution of the study sample according to the socio-demographic characteristics⁻

*DPR: Digital Panoramic Radiography. **CAC: Carotid Artery Calcification.***: Statistically significance (p< 0.05).

	Variable	Normal DPR*		Abnormal DPR (CAC**)		Total		
		n	%	n	%	n	%	<i>p</i> -value
Cigarette smoking:	Yes	68	15.4	16	3.6	84	19	0.184
Mean (\pm SD) = 21.4 (\pm 12.2)	No	286	64.5	50	11.3	336	75.8	
	Former smoker	20	4.5	3	0.7	23	5.2	
Khat chewing:	Yes	159	35.9	30	6.8	189	42.7	0.638
	No	215	48.5	39	8.8	254	57.3	
Coffee & tea drinking:	Yes	335	75.6	64	14.4	399	90	0.608
	No	39	8.8	5	1.2	44	10	
Regular exercise:	Yes	92	20.7	11	2.5	103	23.2	0.127
	No	282	63.7	58	13.1	340	76.8	
Fast food intake:	<5 times /month	301	68	56	12.6	357	80.6	0.507
	2 - 4 /week	52	11.7	11	2.5	63	14.2	
	One time at least	21	4.7	2	0.5	23	5.2	

Table 2. Distribution of the study sample according to the lifestyle.

*DPR: Digital Panoramic Radiography. **CAC: Carotid Artery Calcification.***: Statistically significance (p< 0.05).

	Variable	Nor DP	mal PR*	Abnormal DPR (CAC**)		Total		
		n	%	n	%	n	%	<i>p</i> -value
Previous consultation:	Yes	237	53.5	50	11.3	287	64.8	0.001***
	No	137	30.9	19	4.3	156	35.2	
Previous medication	Yes	269	60.7	55	12.4	324	73.1	0.001***
	No	105	23.7	14	3.2	119	26.9	
Family history	Yes	217	49	47	10.6	264	59.6	0.001***
	No	157	35.4	22	5	179	40.4	

Table 3. Distribution of the study sample according to the medical history.

*DPR: Digital Panoramic Radiography. **CAC: Carotid Artery Calcification.***: Statistically significance (p< 0.05).

RESULTS.

A total of 443 participants were interviewed face to face to obtain their information, and their DPR was assessed for CAC. Distribution of the study sample according to the socio-demographic characteristics is summarized in Table 1. There were more females than males with DPR showing CAC, although this difference was not statistically significance (p=0.933).

Most of the study participants had at least secondary education (364 patients, 82.2%), and 79 patients (17.8%) had completed primary education or less. More than the half of the study sample had enough income (257 patients, 58.0%).The participants ISSN Online 0719-2479 - www.joralres.com © 2019 age and income were the only socio-demographic characteristics which showed statistically significant differences associated with an increased risk of having CAC (p=0.001 and p=0.027) respectively. However, the other socio-demographic characteristics had nonstatistical significance.

Distribution of the study sample according to the lifestyles is summarized in Table 2, which shows that 336 patients (75.8%) were non-smokers, 84 patients (19%) were smokers and only 23 (5.2%) were former smokers. Besides, 189 patients (42.7%) were khat chewers and 254 patients (57.3%) were non khat chewers.

Additionally, 399 patients (90%) were coffee & tea drinkers and 44 patients (10%) were not coffee & tea drinkers. Moreover, 340 patients (76.7%) had not regular physical activity and 103 patients (23.3%) were regular physical activity exercisers. Furthermore, 357 patients (80.6%) regularly ate fast food, and 86 patients (19.4%) seldom ate fast food. The association between formation of CAC and lifestyle variables had non-statistical significance.

Distribution of the study sample according to the medical history is summarized in Table 3, which shows that previous medical consultation involved 287 patients (64.8%), use of medications involved 324 patients (73.1%) and a family history involved 264 patients (59.6%). The association between CAC and the medical history variables were statistically significant (p=0.001).

DISCUSSION.

This study was conducted on 443 Yemeni dental patients to determine the prevalence of CAC detected by DPR as a risk factor for CVDs.

The mean age of the participants of the present study was 46 years old, which was higher than in previous studies.¹⁰⁻¹² Among the different age groups, the present study showed that the age group 41 to 65 years was more likely to have CAC than the other age groups. On contrary, Nasseh *et al.*,⁹ showed a lower correlation between age and CAC at the same age group, and the mean age of participants in their study was 55.6 years old.

In the present study, younger patients with sufficient income had a significantly increased risk of having CAC as a risk factor of CVDs than those with other variables, which is not consistent with other studies that reported the elderly had a higher risk of CVDs.^{13,14}

The current study showed that females were more likely to have CAC visible on DPR than male patients. This finding is inconsistent with that of Qureshi *et al.*,¹⁵ who reported that the male participants were more likely to have CAC on DPR. However this is consistent to the findings of Papakonstantinou *et al.*,¹⁶ and Dick *et al.*¹⁷ Weight had no statistically significant association with the CAC. This finding in disagreement with a study by Chowdhury *et al.*,¹⁸ who found that participants with normal or slightly increased body weight were more likely to develop CAC. Also this study is not in line with Milner *et al.*,¹⁹ as the participant in this study had mostly normal weight due to their lifestyle and type of food consumed.

Several other studies have showed that an increase in serum cholesterol and diabetes can contribute to the development of calcification.²⁰⁻²³ The current study focused on the prevalence of CAC as a clinical problem for patients in Yemeni population. It illustrated that more than half of the participants involved 264 patients (59.6%) complained from cardiovascular-related symptoms. This finding is in agreement with studies by Halwani *et al.*,¹⁴ in Saudi Arabia and Tiihonen *et al.*,²⁴ in Finland.

In the current study, the prevalence rate of CAC was 15.6%, the highest rate in comparison to previous studies by Garoff *et al.*,²⁰ Abreu *et al.*,⁴ Nasseh *et al.*,⁹ Moshfeghi *et al.*,⁵ Taheri *et al.*,²⁵ and Halwani *et al.*,¹⁴ who reported that the prevalence rates of CAC were 5%, 7.9%, 10.2%, 11%, and 12.2% respectively. This may be due to the differences in socio-demographic characteristics, the healthcare awareness of participants, variation in diseases, and differences in sampling methods and techniques.

Although the educational level did not show a statistically significant association with CAC, this study illustrated a trend that the participants with a lower education levels were more likely to developed CAC. On the other hand, participants with higher educational levels had better understanding of the necessity for optimal diet and lifestyle important in preventing CAC that lead to CVDs. This finding is consistent with the study conducted by Poelman *et al.*,²⁶

Similarly, the daily consumption of fast food showed an insignificant association with CAC. However, this habit may lead to obesity, which affects the blood vessels. This finding agrees with Poelman *et al.*,²⁶ and Maidah*et al.*²⁷ Smoking was also not significantly associated with an increased risk of CAC.

However, it was associated with the development of CVD. This finding is similar to other studies such as

those conducted by Halwani *et al.*,¹⁴ and Hirooka *et al.*²⁸ Ceasing smoking is important to prevent the formation of CAC which lead to CVD, as recommended by Patel *et al.*,²⁹ and Seyedmirzaei *et al.*³⁰

The present study showed a significant association between CAC and medical history variables (p=0.001). This result in agreement with previous studies conducted by Halwani *et al.*,¹⁴ and Taheri *et al.*²⁵

Therefore, DPR can be used for early CAC detection which is an indication of asymptomatic CVD, and that could help dentists to make patients avoid any further CVD risk factors.

CONCLUSION.

The prevalence of CAC among Yemeni dental patients was relatively high (15.6%). Patients with asymptomatic CVD can be diagnosed earlier by the detection of CAC by DPR. Female patients have a higher prevalence rate of CAC compared to males. Conflict of interests: Authors declare there is no any conflict of interest

Ethics approval: An ethical approval to carry out this study was granted from the ethical committee of the Faculty of Medicine and Health Sciences, University of Science & Technology (MECA No. 2017/15). The study was explained to all patients and informed consents were anonymously obtained from each patient to confirm their enrollment in the study.

Funding: Self-funded

Author's contribution: The manuscript was written, edited and approved in collaboration between all authors.

Acknowledgements: Authors are sincerely thankful to all academic staff & administrators in the college of dentistry at university of science & technology who helped us to conduct this study.

REFERENCES.

1. Barona-Dorado C, Gutierrez-Bonet C, Leco-Berrocal I, Fernández-Cáliz F, Martínez-González J-M. Relation between diagnosis of atheromatous plaque from orthopantomographs and cardiovascular risk factors. A study of cases and control subjects. Medicina oral, patologia oral y cirugia bucal. 2016;21(1):e66.

2. Madden RP1, Hodges JS, Salmen CW, Rindal DB, Tunio J, Michalowicz BS, Ahmad M. Utility of panoramic radiographs in detecting cervical calcified carotid atheroma. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2007;103(4):543-8.

3. Friedlander AH, Tajima T, Garrett NR. Panoramic radiographs of head and neck cancer patients are often evidence of carotid artery atherosclerotic lesions: a sign of high-risk comorbid illness. J Oral Maxillofac Surg. 2012;70(5):1096-101.

4. Abreu TQ, Ferreira EB, de Brito Filho SB, de Sales KPF, Lopes FF, de Oliveira AEF. Prevalence of carotid artery calcifications detected on panoramic radiographs and confirmed by Doppler ultrasonography: Their relationship with systemic conditions. Indian J Dent Res. 2015;26(4):345.

5. Moshfeghi M, Taheri JB, Bahemmat N, Evazzadeh ME, Hadian H. Relationship between carotid artery calcification detected in dental panoramic images and hypertension and myocardial infarction. Iranian J Radiol. 2014;11(3).

6. Atalay Y, Asutay F, Agacayak KS, Koparal M, Adali F, Gulsun B. Evaluation of calcified carotid atheroma on panoramic radiographs and Doppler ultrasonography in anolder population. Clin Interv Aging. 2015;10:1121.

7. Borba DL, Hipólito UV, Pereira YCL. Early diagnosis of atherosclerosis with panoramic radiographs: a review. Jornal vasc bras. 2016;15(4):302-7.

8. Friedlander AH, Graves LL, Grabich SG, Aghazadehsanai

N, Chang TI. Prevalence of calcified carotid artery atheromas on panoramic images of older men with gout: a descriptive retrospective study. Dentomaxillofacial Radiology. 2017;46(5):20160406.

9. Nasseh I, Aoun G. Carotid artery calcification: A digital panoramic-based study. Diseases. 2018;6(1):15.

10. Morrison BN, McKinney J, Isserow S, Lithwick D, Taunton J, Nazzari H, De Souza AM, Heilbron B, Cater C, MacDonald M, Hives BA, Warburton DER. Assessment of cardiovascular risk and preparticipation screening protocols in masters athletes: the Masters Athlete Screening Study (MASS): a cross-sectional study. BMJ Open Sport Exerc Med. 2018 9;4(1):e000370.

11. Singh A, Collins B, Qamar A, Gupta A, Fatima A, Divakaran S, Klein J, Hainer J, Jarolim P, Shah RV, Nasir K, Di Carli MF, Bhatt DL, Blankstein R. Study of young patients with myocardial infarction: Design and rationale of the YOUNG-MI Registry. Clin Cardiol. 2017;40(11):955-61

12. Roberts JR. InFocus: CV Diseases Most Common Cause of Sudden Death in Young, but Few Have Symptoms to Predict Risk. Emergency Medicine News.2017;39(2):14-16.

13. Bedelbayeva G. Gender and Age Differences with Myocardial Infarction Symptom Presentation and In-Hospital Mortality. Journal of Global Pharma Technology. 2018.

14. Halwani M. Detection of Common Carotid Artery Calcifications in Panoramic Radiographs and its Relationship to Some Chronic Diseases for Local Population in Abha Southern Kingdom of Saudi Arabia -2017-2018: Prevalence and Reliability. International Annals of Medicine. 2017;2(1).

15. Qureshi NA, Hallissey MT, Fielding JW. Outcome of index upper gastrointestinal endoscopy in patients presenting with dysphagia in a tertiary care hospital-A 10 years review. BMC gastroenterology. 2007;7(1):43.

16. Papakonstantinou NA, Stamou MI, Baikoussis NG, Goudevenos J, Apostolakis E. Sex differentiation with regard to coronary artery disease. Journal of cardiology. 2013;62(1):4-11.

17. Dick P, Sherif C, Sabeti S, Amighi J, Minar E, Schillinger M. Gender differences in outcome of conservatively treated patients with asymptomatic high grade carotid stenosis. Stroke. 2005;36(6):1178-83.

18. Chowdhury R, Warnakula S, Kunutsor S, Crowe F, Ward HA, Johnson L, Franco OH, Butterworth AS, Forouhi NG, Thompson SG, Khaw KT, Mozaffarian D, Danesh J, Di Angelantonio E.Association of dietary, circulating, and supplement fatty acids with coronary risk: a systematic review and meta-analysis. Annals of internal medicine. 2014;160(6):398-406.

19. Milner KA, Vaccarino V, Arnold AL, Funk M, Goldberg RJ. Gender and age differences in chief complaints of acute myocardial infarction (Worcester Heart Attack Study). The American journal of cardiology. 2004;93(5):606-8.

20. Garoff M. Carotid calcifications in panoramic radiographs in relation to carotid stenosis: Umeå University; 2016.

21. Jashari F. Carotid artery disease: plaque features and vulnerability: Umeå University; 2015.

22. Hunt KJ, Duggirala R, Göring HH, Williams JT, Almasy L, Blangero J, O'Leary DH, Stern MP. Genetic basis of variation in carotid artery plaque in the San Antonio Family Heart Study. Stroke. 2002;33(12):2775-2780.

23. Lemne C, Jogestrand T, de Faire U. Carotid intima-media thickness and plaque in borderline hypertension. Stroke. 1995;26(1):34-39.

24. Tiihonen J, Lehti M, Aaltonen M, Kivivuori J, Kautiainen H, Virta LJ, Hoti F, Tanskanen A, Korhonen P. Psychotropic drugs and homicide: A prospective cohort study from F inland. World

psychiatry. 2015;14(2):245-7.

25. Taheri JB, Moshfeghi M. Prevalence of calcified carotid artery on panoramicradiographs in postmenopausal women. Journal of dental research, dental clinics, dental prospects. 2009;3(2):46.

26. Poelman M, Strak M, Schmitz O, Hoek G, Karssenberg D, Helbich M, Ntarladima AM, Bots M, Brunekreef B, Grobbee R, Dijst M1, Vaartjes I.Relations between the residential fast-food environment and the individual risk of cardiovascular diseases in The Netherlands: A nationwide follow-up study. European journal of preventive cardiology. 2018:2047487318769458.

27. Maidah AN. Relationship Between Cardiovascular Disease Risk and Fast Food Consumption in Undergraduate Honors College Students. 2014.

28. Hirooka N, Kadowaki T, Sekikawa A, Ueshima H, Choo J, Miura K, Okamura T, Fujiyoshi A, Kadowaki S, Kadota A, Nakamura Y, Maegawa H, Kashiwagi A, Masaki K, Sutton-Tyrrell K, Kuller LH, Curb JD, Shin C. Influence of cigarette smoking on coronary artery and aortic calcium among random samples from populations of middle-aged Japanese and Koreanmen. J Epidemiol Community Health. 2013;67(2):119-124.

29. Patel YR, Gadiraju TV, Ellison RC, Hunt SC, Carr JJ, Heiss G, Arnett DK, Pankow JS, Gaziano JM, Djoussé L. Coffee consumption and calcified atherosclerotic plaques in the coronary arteries: The NHLBI Family Heart Study. Clinical nutrition ESPEN. 2017;17:18-21.

30. Seyedmirzaei SM, Haghdoost AA, Afshari M, Dehghani A. Prevalence of dyspepsia and its associated factors among the adult population in southeast of Iran in 2010. Iran. Red Crescent Med J. 2014;16(11).