CAROTID ARTERY ATHEROMAS AND CALCIFICATIONS AMONG POSTMENOPAUSAL WOMEN WITH DIABETES AND HYPERTENSION

*Asmaa T Uthman[3], Lamya Al-Naqeeb[2], Baydaa Al-Saleem[2], Natheer Al-Rawi[1]**

1.MSc , College of Dental Medicine , Ajman Gulf Medical University, UAE.
2. M.Sc , College of Dentistry,University of Baghdad, Iraq.
3. PHD, College of Dentistry, University of Sharjah, UAE.

Abstract

Hypertension and diabetes are the most important disorders correlated with carotid artery atheromas or calcification. The measurement of actual atheroma or volume can probably provide an accurate and comprehensive view of the extent and severity of atherosclerosis. Forty- five consented post menopausal Iraqi women were recruited in this study,thet were grouped into three groups of equal numbers; control group, diabetic group and hypertensive group. All participants underwent ultra- sonographic assessment of the carotid arteries region for the detection of any stenosis and a dental panoramic imaging for the detection of carotid calcification of the right and the left side.The aim of this study was to evaluate the presence of carotid artery stenosis with or without calcification among postmenopausal women with hypertension or diabetes.Carotid artery calcifications (CACs) were detected in 12 arteries, 2 of which had significant stenosis in the diabetic group. In the hypertensive group, 4 arteries were calcified with no significant stenosis as seen on Doppler ultra- sonography (DUS) . The prevalence ratio was 1.7 for the hypertensive group and 1.3 for the diabetic group. The ratio of significant stenosis patients with CACs on either side was high enough to necessitate the use of DUS as a cost- effective screening method and as a life-saving measure for postmenopausal women at a high risk of vascular diseases.

Clinical article (J Int Dent Med Res 2014; 7: (2), pp. 42-48)

Keywords: Carotid artery calcifications, Carotid artery stenosis, Postmenopausal, Sonography.

Received date: 12 February 2014 **Accept date:** 14 March 2014

Introduction

Carotid atheroma is an atherosclerotic disease process that occurs along the wall of the lumen of common carotid artery (CCA) near its bifurcation. Pieces of atheromas may ulcerate and break off to form an embolus that can occlude a smaller intra cerebral artery leading to stroke.[1] Arterial narrowing exerts a profound effect on the arterial blood flow because the resistance varies inversely with the fourth power of the luminal radius. [2] Vascular calcification has been suggested as a surrogate marker of atherosclerosis. [3] Calcification of carotid bifurcation region is detectable on dental panoramic imaging (DPI) in 1 -5% of the adult population.[4] Calcification is a morphological complication in the evolution of atheromatous plaque (AP). Generally, carotid artery calcifications (CACs) are found at the branch point of artery vessels where the turbulent flow is increased. [5]

Hypertension and diabetes are the most important factors correlated with CACs. A history of hypertension was frequently noted in patients with cerebral thrombosis and it is commonly present in patients with intra- cerebral hemorrhage. [6] Damrongsri and Thanakun found that hypertension was associated with the presence of CACs in postmenopausal women.[7] Type 2 diabetes is a disease complex with both metabolic and vascular components that accelerate the development of atherosclerotic lesions at the bifurcation of the CCA and double

Corresponding author:
Dr. Natheer H AL-Rawi
College of Dentistry, University of Sharjah,
Sharjah, UAE
PO Box: 27272
Fax:+97165585641
Phone: 00971505307689
E-mail: nhabdulla@sharjah.ac.ae

or triple the risk of ischemic stroke [8] . Increased risk of stroke because of hyperglycemia, hyperlipidemia and hypertension have been implicated as the cause of premature atherosclerosis of the cervical portion of the carotid artery. [9] Levels of low-density lipoprotein –cholesterol (LDL-C) and high – density lipoprotein – cholesterol(HDL-C) are the primary determinants of the risk of atherosclerosis and heart attack among both men and women.[10] There are changes in lipid around the time of the menopause. The Health Women Study found a small, but significant, decrease in the HDL level and a substantial increase in the LDL and total cholesterol levels at the time of menopause.[11] Post- menopausal women had 4 – 5 times greater odds of plaque as compared with premenopausal women. [12] Friedlander and Altman reported that the decline of estrogen in menopause women increases the LDL levels in the blood which in turn causes hardening and thickening of the vessel walls .[5] The carotid arteries are of particular interest to investigators because they are easily accessible to non-invasive examination by ultra-sonography (US). [13] Carotid (US) is now the principal screening technique to assess the suspected extra-cranial carotid atherosclerotic disease.[14] The intima medial thickening (IMT) of the CCA measured by external vascular US is often used as a marker for coronary atherosclerosis. The measurement of actual plaque atheromas or atheroma volume can probably provide a more accurate and comprehensive view of the extent and severity of atherosclerosis. [15] The purpose of this study was to evaluate the presence or absence of carotid artery stenosis with or without calcification among postmenopausal women with hypertension or diabetes using DUS and DPI.

Methods

A prospective study was performed on 45 consented postmenopausal Iraqi women from the Baghdad Medical Teaching Hospital. The medical ethical committee of the hospital approved the study. The study subjects were divided into 3 groups: Control, hypertensive (HT), and diabetic (DM) groups. The control group comprised 15 healthy postmenopausal women with normal clinical (ECG and blood pressure) and biochemical(Lipid profile and fasting blood glucose) investigations. The HT group consisted of 15 postmenopausal women suffering from hypertension only. The DM group consisted of 15 postmenopausal women suffering from type 2 diabetes (FBG>7 mmol/L).

Imaging Procedure:

Prior to DPI and DUS examination, the heart rate, electrocardiogram (ECG), and blood pressure were recorded together with the biochemical assessment of lipid profile and fasting blood glucose levels. All subjects underwent panoramic radiographic imaging with the Planmeca Prolin CC Unit (6 - 9 mA and 60 - 70 kVp). To visualize the carotid area, the patient was made to stand 1- cm anterior and 1- cm posterior to the normal standard position. [16] Radiographic observations of (CACs) were done. A radiopaque shadow of irregular, heterogeneous, nodular mass or masses or two vertical radiopaque lines located 1.5 cm inferior and 2.5 cm posterior to the cortical rim of mandibular angle at the level of cervical vertebrae (C1, C2 and C3) were considered as CACs (figure 1).

Figure (1): Bilateral Carotid artery calcification

Lymph nodes calcification, calcified triticeous cartilage and phleboliths were excluded. For sonographic examination, bilateral arterial DUS was performed by using Siemens Doppler Ultrasound G40 unit with a 5- MHz linear array imaging probe. Each examination was performed by an experienced sonographer.

Hemodynamic criteria: The sonographer recorded the highest angle-adjusted peak systolic velocity (PSV) and peak end diastolic velocity (PEDV) of erythrocytes within the (CCA) and the internal carotid artery (ICA) of both sides. The ratio of PSV for ICA/PSV for CCA and PEDV for ICA/PEDV for CCA were also recorded (figure 2).

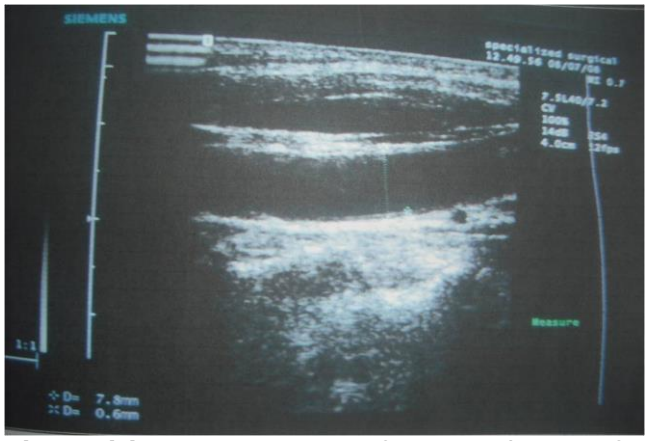

Figure (2): Measurements of PSV and PEDV for carotid artery.

For morphological appearance of the examined arteries, the reduction of the lumen diameter of ICA and CCA was observed using longitudinal plane of the examined artery. The reduction of the lumen area of ICA and CCA were measured using the transverse plane of the examined artery. [17] (figure 3).

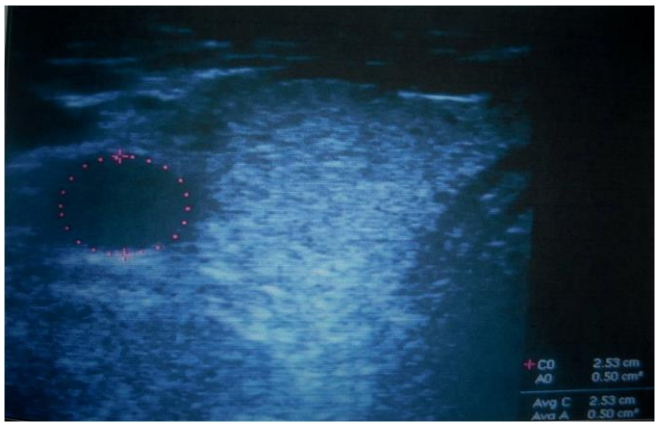

Figure (3): Measurements of normal diameter of common carotid artery using longitudinal plane.

The following percentages were obtained

1. Percentage of linear stenosis =
   {1 - (r/n)} x 100

Where, n = normal diameter of the artery and
R = residual diameter of the artery.

2. Percentage of area stenosis =
   {1 - (Ar/An)} x 100

Where, An = area of the normal lumen and
Ar = area of the residual lumen.

Direct atherosclerosis assessment was also measured for both ICA and CCA using the B- mode ultrasound in the longitudinal plane with minimum gain necessary to clearly visualize the lumen .[18] (figure 4).

Significant carotid artery stenosis was defined as stenosis ≥ 50%.[19] According to the current guideline for significant stenosis [16], the final diagnosis of significant stenosis (FDSS) was determined by using 2 outcomes of 6 DUS criteria, which were used to determine significant stenosis (i.e , >50%).

The six criteria used in this study included the following:

- PSV >120 or <25
- PEDV > 40
- PSV ratio > 1.99
- PEDV ratio > 2.6
- Percent linear stenosis > 49.9%
- Percent area stenosis > 49.9% [16]

The statistical significance of differences in velocity measurements along the course of ICA and CCA were assessed using the two tailed student t-test and ANOVA, and $p \leq 0.05$ was considered statistically significant.

The Mann –Whitney test was also used to explore the significance of differences in the median of non-normally distributed quantitative variables (ratios) between the studied groups.

The prevalence ratio (PR) was calculated to measure the risk of having CAC in DPI in the study group compared to the healthy control.[20] The performance characteristics (validity) of a test like sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were also assessed using SPSS version 17 (Chicago, IL).

Results

A total of 45 post menopausal Iraqi women were included in this study. The mean age ranged from 53 to 60 years; all subjects had the body mass index (BMI) between 24.6 and 26.4 kg/m^2.

Table (1) demonstrated carotid atheroma and its relation with the presence or absence of CACs. All the 30 examined sites in the control group were negative for CACs on DPI; this was confirmed by 3 expert maxillofacial radiologists.

These 30 sites had negative DUS findings with regards to the carotid AP. In the HT group, 8 sites were positive for CACs on DPI. Among the 8 positive sites, three sites had positive DUS finding with regards to AP. In the DM group, 8 sites were positive for the CACs, of which 6 had positive DUS findings.

Groups	Carotid AP by DUS				%
HT group					
Panoramic X-ray evidence of CACs	Negative	Positive	Total	Sensitivity	75
				Specificity	80.8
Negative	21	1	22	Accuracy	80
Positive	5	3	8	PPV	37.5
Total	26	4	30	NPV	95.5
DM group					
Panoramic X-ray evidence of CACs	Negative	Positive	Total	Sensitivity	60
				Specificity	90
Negative	18	4	22	Accuracy	80
Positive	2	6	8	PPV	75
Total	20	10	30	NPV	81.8

Table 1. Diagnostic performance of CACs observed by DPI in predicting AP observed by DUS

The value of a positive test result in establishing the presence of an outcome is expressed as the PPV.

The PPV was higher in the DM group (75%) than in the HT group (37.5%), suggesting that patients with radiographic evidence of CACs had AP (as detected by DUS) with 75% confidence among diabetic patients , but only 37.5% confidence in HT patients .

When CACs was observed on DPI, the FDSS was also assessed.

In the HT group, no site with FDSS was detected. In the DM group, 5 sites had FDSS, including 2 with CACs (as detected by DPI), which made the NPV as 85% (Table 2). Moreover, we noted that patients with HT or diabetes, who were positive for AP (as detected by DUS) had FDSS with 86.7% and 63.3% accuracy, respectively.

Groups	FDSS				%
Control group					
Panoramic X-ray evidence of CACs	Negative	Positive	Total	Specificity	100
Negative	30	0	30	Accuracy	100
Positive	0	0	0	PPV	0
Total	30	0	30	NPV	100
HT group					
Panoramic X-ray evidence of CACs	Negative	Positive	Total	Specificity	86.7
Negative	26	0	26	Accuracy	86.7
Positive	4	0	4	PPV	0
Total	30	0	30	NPV	100
DM group					
Panoramic X-ray evidence of CACs	Negative	Positive	Total	Sensitivity	40
				Specificity	68
Negative	17	3	20	Accuracy	63.3
Positive	8	2	10	PPV	20
Total	25	5	30	NPV	85

Table 2: Diagnostic performance of AP in predicting FDSS detected by DUS

Regarding the DUS diagnostic criteria used for determining the significant stenosis, we found that 5 patients in the HT group (33.3%) had PSV >120, with no patient with PEDV >40. No linear or area stenosis was detected in this group. All had carotid atheroma plaque (as detected by DUS), 3 of which demonstrated evidence of calcification on DPI.

Regarding the DM group, only 6 had PSV >120, of which only 2 had PEDV >40 , 3 had PSV ratio >1.99 and PEDV ratio >2.6, and only 1 had percent linear stenosis >49.9.

Four out of the 6 diabetic patients with the significant stenosis showed evidence of CACs (Table 3).

It is worth mentioning that the PR of positive AP, as detected by DUS, was 33.3% in the HT group and 26.7% in the DM group.

The risk of being positive for CACs, as detected by DPI, was 1.7- times more for the HT group and 1.3- times more for the DM group as compared to the healthy control group as measured by the PR.

Significant stenosis determined by:	Control group (n = 15)			HT group (n = 15)			DM group (n = 15)		
	N	%	95% CI for PR	N	%	95% CI for PR	N	%	95% CI for PR
PSV >120	0	0		5	33.3	9.2 - 57.4	6	40	15 - 65
PEDV >40	3	20	0 - 40.4	0	0		2	13.3	0 - 30.7
PSV ratio >1.99	1	6.7	0 - 19.5	0	0		3	20	0 - 40.4
PEDV ratio > 2.6	2	13.3	0 - 30.7	3	20	0 - 40.4	3	20	0 - 40.4
Percent Linear stenosis >49.9%	0	0		0	0		1	6.7	0 - 19.5
Percent area stenosis >49.9%	0	0		0	0		0	0	
Any of six criteria	5	33.3	9.2 -57.4	8	53.3	27.8-78.9	9	60	35 - 85
At least two of six criteria	1	6.7	0 - 19.5	0	0		5	33.3	9.2 - 57.4
Stenosis determined by:									
Carotid abnormal plaque by DUS	0	0		3	20	49.2 - 57.4	6	40	15-85
Panoramic X-ray evidence of carotid atheroma	0	0		5	33.3		4	26.7	4.1 - 49.3

Table 3: PRs of positive criteria for significant stenosis

The risk of being positive for FDSS was the highest in the DM group (Predictive Ratio for FDSS was positive in five patients. However, none of the HT group was positive for FDSS as detected by DUS (Table 4).

Group	Total	Carotid AP by DUS			Panoramic X-ray evidence of CACs					FDSS				
	N	N	%	P Fisher's	N	%	PR	95% CI	P Fisher's	N	%	PR	95% CI	P Fisher's
HT	15	3	20	0.22 (NS)	5	33.3	1.7	0.5 - 5.8	0.68 (NS)	0	0			
DM	15	6	40	0.02 *	4	26.7	1.3	0.3 - 0.8	1 (NS)	5	33.3	5	0.7-9	0.17 (NS)

Table 4: Risk of being positive for selected outcomes

Discussion

The physiological changes associated with menopause, such as reduced levels of estrogen and other processes associated with aging, result in women being at a disproportionately high risk of developing carotid artery atherosclerosis , because they frequently develop an atherogenic blood profile at the time of menses cessation[7] .

When atherosclerotic lesions are partially calcified, they can be observed via panoramic radiography.[21,22] Bayram et al [23] concluded that dental panoramic tomography may have some diagnostic value for detecting CACs and that early diagnosis can potentially increase the length and improve the quality of life of people with CACs.

Cohen et al.[24] proposed three explanations for why CACs appear to carry an ominous cerebrovascular and cardiovascular prognosis. Specifically, these calcifications may be a sign of underlying carotid stenosis ,and an indication of a heavy risk - factor burden or an independent factor for cerebrovascular or cardiovascular diseases. Early identification of stroke-prone patients and referring them to a physician for a cerebrovascular and cardiovascular work-up as part of an active stroke prevention strategy will greatly reduce the disease morbidity and mortality. However, panoramic radiography is limited to the identification of the atheromas, and it cannot evaluate its exact location and the degree of occlusion. Contrast angiography is therefore used for the confirmation of the presence of calcification, its nature, and its extension. [21] However, the high cost, the potential serious complications, and the limited information obtained by this method has stimulated the development of non - invasive techniques, such as DUS.[25]

Increased risk of stroke because of hyperglycemia, hyperlipidemia and hypertension, often associated with the disorder has been implicated as a cause of premature atherosclerosis of the cervical portion of the carotid artery and to markedly increase the incidence of ischemic stroke.[9]

Almog et al.[4] found that the calcifications near the carotid bifurcations on panoramic radiograph cannot be proposed as a a trigger for cost-effective US.

In the present investigation, CACs were observed in 12 arteries, of which 2 had significant stenosis in the diabetes group with 40% sensitivity. However, in the HT group, 4 calcified arteries was detected without any significant stenosis, and 3of the 17 examined non-calcified arteries had significant stenosis (>50%) on DUS, this significant stenosis without calcification can be explained on the basis that the atheromas causing the stenosis was not yet calcified and could not been seen on dental panoramic tomography .

Carotid abnormal plaque was also evident in 3 HT patients and 6 diabetic patients by DUS. Neschis et al [26] studied the criteria determined for the detection of ≥50% carotid artery stenosis, and found the highest accuracy and sensitivity for PSV of 170cm/s and PEDV of > 60 cm/s in the ICA.However, PSV in this study did not exceed 170cm/s owing lower accuracy, specificity, and PPV when compared with the findings of Neschis et al (data not shown), [26] and the PRs of CACs in this study were between 1.3-1.7 in the studied groups.

The findings of Giorda et al.[27]in a stroke prevention and educational awareness diffusion collaboration study, is in accordance with our finding about the higher PR of FDSS (which is the risk of stenosis that may lead to stroke) in the type 2 diabetes group (5- times greater than that of the control group).

De Angelis et al.[28] studied the prevalence of carotid stenosis in cerebrovascular- disease- free type 2 diabetic patients. Diabetic patients were three times more likely to develop carotid stenosis than the non-diabetic patients. [28]

Fukuta et al.[29] reported 29.3% of patients with CACs , and an incidence rate 14.7- times higher in them than that in patients without CACs. The natural progression of median carotid stenosis showed no changes over 4 years in asymptomatic patients undergoing recommended therapy .[30]

According to the finding of the present study, we suggested that diabetic and hypertensive menopause women might be at a risk of developing carotid artery stenosis that might predispose to CVA.

Conclusion

The ratio of significant stenosis with or without CACs was high enough to advocate the use of DUS as a cost-effective screening method and as a life-saving measure for menopause women at high risk of vascular diseases, we suggest that a one-time screening program could be recommended for diabetic patients with carotid bruit or with coronary disease (as secondary prevention) and for all patients over 60 years of age, who smoke and have hypertension and/or abnormal lipid profile levels

References

1. Madden RP, Hodges JS, Salmon CW, et al. Utility of panoramic radiographs in detecting cervical calcified carotid atheroma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007; 103(4):543-8.
2. Rhoades RA, Tanner GA. Medical Physiology. 2nd Ed 2000.Boston: Little Brown.
3. Fanning NF, Walter TD, Fox AJ, Symons SP. Association between calcification of the cervical carotid artery bifurcation and white matter ischemia. Am J NeuroRadiol 2006;27:378-83
4. Almog DM, Horev T, Illig KA, et al. Correlating carotid artery stenosis detected by panoramic radiography with clinically relevant carotid artery stenosis determined by duplex ultrasound. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002; 94(6):768-73.
5. Sun Z. Hemodynamic effect of calcified plaque on blood flow in carotid artery disease: A preliminary study. Bioinform Biomed Eng 2009.ICBBE 2009, 3rd International Conference.
6. Sahni R, Weinberger J. Management of intracerebral hemorrhage. Vas Health Risk Manag 2007;3(5):701-9.
7. Damrongsri SP, Thanakun S. Carotid artery calcification detected on panoramic radiographs in a group of Thai population. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006; 101(1):110-5.
8. Banerjee C, Moon YP, Paik MC et al. Duration of diabetes and risk of ischemic stroke. The Northern Manhattan Study. Stroke 2012;111:641381.
9. Kodoglou NP, Iliadis F, Liapis CD. Exercise and carotid atherosclerosis. Eur J Vas Endovas Surg. 2008;35(3):264-72.
10. Vergeer M, Holleboom AG, Kastelein JJ, Kuirenhoven JA. The HDL hypothesis: Does high density lipoprotein protect from atherosclerosis? J lipid Res 2010;51(8):2058-73.
11. Matthews KA, Crawford SL, Chea CU. Are changes in cardiovascular disease risk factors in midlife women due to chronological aging or to the menopausal transition? J Am Col Cardiol 2009;54(25):2366-73.
12. Tamura T, Inui M, Akase MN, et al. Clinico statistical study of carotid calcification on panoramic radiographs. Oral Dis 2005; 11:314.
13. Slovut DP, Romero JM, Hannon KM, Dick J, Jaff MR. Detection of common carotid artery stenosis using duplex ultrasonography: a validation study with computed tomographic angiography. J Vas surg 2010;51(1):65-70.
14. Allan PL, Dubbin PA,Pozniak MA, McDicken WN. Clinical Doppler ultrasound. 2nd Edition , Churchil Livingstone,2002.
15. Spence JD. Ultrasound Measurement of carotid plaque as a surrogate outcome for coronary artery disease. MD Am J Cardiol 2002; 89:10-16.
16. Farman AG. Panoramic radiology and the detection of carotid atherosclerosis. Pan Imaging News 2001; 1(2):1-5.
17. Koga M, Kimura K, Minematsu K, et al. Diagnosis of internal carotid artery stenosis greater than 70% with power Doppler duplex sonography. AJNR AM J Neuroradiol 2001; 22:413-7.
18. Riccio SA, House AA, Spence JD, et al. Carotid ultrasound phenotypes in vulnerable populations. Cardiovasc Ultrasound 2006; 4:44.
19. Halliday A,Mansfield A,Maro J, et al. Asymptomatic Carotid Surgery Trial (ACST) Collaborative group. Lancet 2004;363(9420):149.
20. Kishikawa K, Kamouchi M, Okada Y, et al. Evaluation of distal extracranial internal carotid artery by transoral carotid ultrasonography of patients with severe carotid stenosis. AJNR AM J Neuroradiol 2002; 23(6):924-8.
21. David MP, Usha VA. Prevalence of carotid artery atheromas in post menopausal women: A digital panoramic radiographic study. J Ind Acad Oral Med & Radiol 2013;25(2):1-6.
22. Uthman AT, Al-Saffar AB. Prevalence in digital panoramic radiographs of carotid area calcification among Iraqi individuals with stroke-related disease. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008;105(4):e68-73.

23. Bayram B, Uckan S, Acikgoz A, et al. Digital Panoramic radiography: a reliable method to diagnose carotid artery atheromas? Dentomaxillofacial Radiol 2006; 35(4):266-70.
24. Cohen SN, Friedlander AH, et al. Carotid calcification on panoramic radiographs: an important marker for vascular risk. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002; 94:510-14.

25. Friedlander AH, Friedlander IK. Panoramic dental radiography: an aid in detecting individuals prone to stroke. Br Dent J 1996; 181:23-26.
26. Neschis DG, Lexa FG, Davis JT, et al. Duplex criteria for determination of 50% or greater carotid stenosis. J Ultrasound Med 2001; 20(3):207-15.
27. Giorda CB, Avogaro A, Maggini M, et al. Incidence and risk factors for stroke in type 2 diabetic patients. Stroke 2007; 38:1154-60.
28. De Angelis M, Scucca L, Leandri M et al. Prevalence of carotid stenosis in type 2 diabetic patients asymptomatic for cerebrovascular disease. Diab Nutr Metab 2003; 16:48-55.
29. Fukuta Y, Kimura T, Totsuka M. Oral findings of patients with cardiovascular disease: remaining tooth number and panoramic radiographic findings. Jpn J Oral Diag Oral Med 2003; 16:15-21.
30. Sleight SP, Polonieck J, Halliday AW.Asymptomatic carotid surgery trial corroborators. Asymptomatic carotid stenosis in patients on medical treatment alone.Eur J Vasc Endovasc Surg 2002; 23:519-23.