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Correlation of Carotid Artery Calcifications in Postmenopausal Women with Periodontitis: A Cross-Sectional Digital Panoramic Radiographic Study in East Godavari Population

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Abstract: The prevalence of cardiovascular diseases, especially atherosclerosis-related incidents, is a significant cause of mortality worldwide. This study aims to investigate the correlation between carotid artery calcifications (CAC) detected through panoramic radiographs and Doppler ultrasonography in postmenopausal women with periodontitis.

Cardiovascular diseases, particularly atherosclerosis, are leading causes of death, often involving calcium-rich fatty plaques on artery walls. This study focuses on the detection of CAC, a marker for cardiovascular events, in postmenopausal women. Menopause-associated hormonal changes increase the risk of stroke, particularly ischemic cerebral injuries due to atherosclerosis.

The research involves 1,257 postmenopausal women over 45 years with periodontitis. Periodontitis contributes to inflammation and may enhance atherosclerosis. Digital panoramic radiographs are used to assess alveolar bone loss through the Progressive Rate Index (PRI). Carotid artery calcifications are also identified on panoramic radiographs and further confirmed through Doppler ultrasonography.

Results reveal that patients with higher PRI values have more severe periodontitis and increased prevalence of CAC. Panoramic radiographs accurately predict CAC presence, as confirmed by ultrasonography. Sensitivity is 85.71%, and specificity is 100%. Identifying CAC through panoramic radiography prompts early intervention and prevention strategies.

This research highlights the potential of panoramic radiographs in detecting CAC and predicting cardiovascular risks in postmenopausal women with periodontitis. The study underscores the importance of interdisciplinary collaboration between oral physicians and radiologists in identifying cardiovascular risks and prompting appropriate management. Further investigations could enhance the reliability of panoramic radiography in CAC identification.

Keywords: Atherosclerosis, Menopause, Panoramic digital radiographs, Periodontitis.

I. INTRODUCTION

Cardiovascular disease and the cerebrovascular incidents are considered to be one of the most frequent causes of death with atherosclerosis being considered as the leading pathology. Atherosclerosis is characterized by the formation of calcium-rich fatty plaques on the walls of arteries either diffusely and/or localized and thus resulting in narrowing and hardening of the arteries. This is associated with accumulation of fat in the artery walls known as atheroma. Silent calcifications in cardiac vessels such as common carotid artery will result in the development

of stroke, peripheral artery disease, myocardial infarction and other thromboembolic events. Most common factors that facilitate atherosclerosis are aging, hypertension, obesity, hypercholesteremia, diabetes mellitus, physical inactivity, sedentary lifestyle, poor eating habits, cigarette smoking, coronary artery disease etc (1). Coronary heart disease (CHD) is a major cause of mortality and morbidity all over the world and attributes to about 13.2 percent of all deaths. 17.5 million People die each year from CVD, an estimated 31% of all deaths worldwide. 80% of all CVD deaths are due to heart attacks and strokes. In India, there is an alarming increase over the past two decades in the prevalence of CHD and cardiovascular mortality (2).

Menopause is a physiological change observed in women with aging and is associated with hormonal and body changes, thus exposing women to a disproportionately high risk of developing stroke (1). In most instances, strokes in postmenopausal women are the result of ischemic cerebral injury caused by atherosclerotic disease. Menopause seen in the fifth decade of a woman's life is characterized by a diminution in estrogen output secondary to reduction of follicular function (1). Reduced levels of circulating estrogen are associated with an increase in hepatic lipase activity and a decrease in LDL catabolism which results in increased levels of LDL and decreased levels of HDL (3).

Calcium salts are taken up by the vessel wall during the maturation process of atheromas resulting in radio-opacities on radiographs. Panoramic radiographs show these calcified carotid atheromas and are powerful markers for future cardiovascular and cerebrovascular disasters and death. Early detection of patients at risk of cardiovascular or cerebrovascular events is critical for application of preventive strategies and management protocols (4, 5).

A significant proportion of strokes are ischemic in nature, attributed to carotid bifurcation atherosclerosis that occurs due to the gradual accumulation of fatty deposits, macrophages, and scar tissue in the artery walls, leading to the formation of atherosclerotic plaque (6). Atherosclerotic plaques are not static lesions; they undergo dynamic changes in their size and morphological characteristics. These changes manifest themselves as changes in plaque volume and consistency, otherwise known as plaque progression and regression. These, together with adaptive responses of the arterial wall, determine the degree of stenosis in the diseased artery. This degree of stenosis is the measurable clinical finding which, together with timing and nature of symptoms and co-morbidities, correlates with the risk of developing further vascular events (7, 8).

The prevalence of cardiovascular diseases in patients with periodontitis is 25–50% higher than in healthy individuals. Inflammatory process stimulated by periodontal and infectious etiology has been associated with development and progression of atherosclerotic plaques. Poor oral health, a potential risk factor for periodontitis and tooth loss are strongly associated with atherosclerotic changes in major blood vessels. Several investigation modalities are available to delineate these atheromatous changes and calcification in blood vessels. Doppler ultrasound is the most important imaging modality for preoperative assessment of patients with the carotid atherosclerotic disease. It is non-invasive, relatively inexpensive and very accurate at the identification of significant ICA stenosis. In measuring the degree of stenosis, the flow and velocity characteristics assessment Doppler effect is utilized. Doppler devices also generate high resolution B-mode ultrasound images of the atherosclerotic lesion. These images contribute significantly to the assessment of carotid plaque instability and correlation with the development of ischemic events (9, 10).

Therefore, through our study, we aim to elucidate and correlate the detection of the carotid artery calcifications in postmenopausal women with periodontitis on panoramic radiographs and confirming these findings with more appropriate imaging modality Doppler ultrasonography.

II. Materials & methods:

The subjects screened are the post-menopausal women above the age of 45 years visiting the Department of Oral Medicine and Radiology, Lenora Institute of Dental Sciences and the Lenora Rural Hospital, Rajanagram, East Godavari (Dist) Rajahmundry for a period of 21 months that is from January 2015 to September 2016. Study subjects included are post-menopausal women above the age of 45 years with periodontitis excluding male

patients, female patients below 45 years of age and female Patients above 45 years with neither menopausal history nor periodontitis. The study was conducted after obtaining ethical clearance from the institutional ethical committee. All the subjects were explained about the study in the language known to them and an informed consent was obtained.

A detailed case history along with thorough clinical examination, of all the post-menopausal female patients of age above 45years was recorded.

Periodontitis was assessed based on the presence of any of the following criteria:

- The depth of gingival sulcus**:**> 3mm.
- Apical migration of marginal gingiva below the level of cement-enamel junction>2mm.
- Tooth mobility**:** >1mm.

Digital panoramic radiographs using The PLANMECA 2002 PROLINE panoramic x-ray unit were taken at exposure parameters of 18 sec, 73 kV and 12mA on a phosphor plate digital receptor of size 15X30 cm. Radiographs were examined for assessing the alveolar bone loss and carotid artery calcifications in subdued ambient light by two radiologists who are blindfolded of each other.

The digital panoramic radiographs were used to assess alveolar bone loss using the PRI (progressive rate index) as described by Craft et al. All the calculations are performed using AGFA HEALTHCARE imaging software at a spatial resolution of 10 pixels/mm and a pixel matrix of 1440X2928. 6 teeth are used in assessing PRI. The 6 teeth indices include the mesial surface of the maxillary and mandibular first molars, second premolars, and central incisors. In cases of missing or unreadable teeth, the most clearly observed next tooth surface in the same sextant is used as a replacement. If the measurements are impossible for 1 or 2 sextants for a given patient, the sum of 4 measurements from their respective sextants is used in the conversion to percent bone loss using the formula below**:**

The % of bone loss for each tooth = (distance from CEJ to alveolar crest-1/root length) X 100

Total bone loss = Σ bone loss / total no of teeth

∑=Sum of bone loss of index teeth

Then the digital panoramic radiographs were evaluated for carotid artery calcifications in the region of carotid artery bifurcation which was taken at the level of the lower margin of the third and entirety of the fourth cervical vertebra, i.e. About 1.5 to 2.5 cm inferior- posterior to the angle of the mandible.

Patients showing carotid artery calcifications in digital panoramic radiograph were further assessed with PHILLIPS Duplex Doppler HD7 XE Ultrasound machine. Ultrasonographic studies were performed with scanners that incorporated with a high-frequency transducer at 5 - 7.5 MegaHertz. Interpretation of the Doppler images was evaluated by experienced general radiologists for the presence of atherosclerotic plaques and carotid artery calcifications (Figure 1, 2, 3, 4). All the obtained values & observations were tabulated and subjected to statistical analysis.

III. STATISTICAL ANALYSIS:

The analysis was done using SPSS 18 version using student t-test and Kappa coefficient. A p-value of <0.05 was considered statistically significant.

IV. Results:

Postmenopausal women above 45 years with periodontitis visiting the Department of Oral Medicine and Radiology, Lenora Institute of Dental Sciences and the Lenora Rural Hospital, Rajahmundry for a period of 21 months were included in the study. The total number of patients examined and screened were 1, 12,757 (Table 1) with a mean and standard deviation of 233.2 ±67. 115.5 ±29.9 were males and 111±29. The total numbers of female patients above 45 years were 10.2 ±7.6 respectively (Table 1) and out of this 978 patients had attained menopause (1.93±2). Age of postmenopausal women showing carotid artery calcification was 50.47±4.8 and subjects without carotid artery calcification were 51.8±5.2.

Out of the 978 post-menopausal female population who are above the age of 45 years, 250 showed periodontitis (Table 2). Percentage of postmenopausal females with periodontitis was assessed to be 16.80%. The age of these post-menopausal female patients with periodontitis ranged from 46-72 years who were divided into three groups, whose PRI (Progressive Rate Index) was evaluated on digital panoramic radiographs. The total numbers of patients in the age range of 46-55 years were 205, with the PRI of 28.1±9.2. The subjects in the age range of 56-65 years were 41 had PRI of 25.5±6.3. The subjects in the age range of 66-75 years were 4 with PRI of 28.6±9.6. (Table 3)

The digital panoramic radiographs of these patients were evaluated for carotid artery calcifications (CAC) in the region of carotid artery bifurcation which was taken at the level of the lower margin of the third and entirety of the fourth cervical vertebra. The total number of positive cases with carotid artery calcifications were 19, out of which 13 (68.42%) were bilateral and 6 (31.57%) were unilateral (Table 4).

These 19 post-menopausal women with periodontitis and positive carotid artery calcifications showed similar findings in ultrasonography (Table 5) The study had a sensitivity of 85.71% and specificity of 100% for determining the inclusion of digital panoramic radiograph for detecting carotid artery calcifications. Positive predictive value was 100 and Negative predictive value 92.31 (Table 6).

V. Discussion:

Women are normally protected against atherosclerosis and cardiovascular diseases but with the onset of menopause, the reducing estrogen levels facilitate atheroma formation in blood vessels. This increases the incidences of cardiovascular and cerebrovascular events in women in old age. According to several studies, vascular calcification and structural aging may predispose an individual towards the development of osteoporosis in bones, thus resulting in periodontal diseases (8, 11).

In this study 250 female postmenopausal above 45 years, who showed periodontitis (Table 2) were screened and enrolled in the study. These elderly female patients who are identified to have periodontitis and also attained menopause are prone to develop stroke and hence these patients are selected and evaluated for the CAC and PRI.

These 250 female patients of age group 53.3±8.2years were subjected to digital panoramic radiograph and PRI was calculated to assess the bone loss and further evaluated for CACs. The percentage of alveolar bone loss in panoramic radiographs can be estimated by the use of Progressive Rate Index (PRI) (12).

The 250 patients were divided into 3 age groups. The total numbers of subjects in the age range of 46-55 years were 205, with the PRI of 28.1±9.2mm, the subjects in the age range of 56-65 years were 41, with the PRI of 25.5±6.3mm and the subjects in the age range of 66-75 years were 4, with PRI of 28.6±9.6. Depleted estrogen increases the bone resorption by increasing the osteoclast number and osteoclast activity thus contributing to the periodontal bone loss (13). The more the PRI index the greater will be the bone loss and severe would be the periodontitis. In our study, the first (46-55 years) and the third (66-75 years) groups showed more PRI values when compared to the second group (56-65 years).

In postmenopausal females, depletion of the estrogen levels will be evident which alters the RANKL concentration, the key protein essential in the prevention of aortic calcification (14). There were very few reported studies done in South Indian population investigating the prevalence of the carotid calcifications. When we evaluated these 250 patients for CAC we followed the method of 8 and 11 boxes as quoted by Janisha Vengalath et al (15). In our study out of 250 patients who had periodontitis, 19 patients had calcifications on panoramic radiographs with the prevalence of 7.6%. Taheri et al (39) detected 22 CAC out of 200 radiographs of post-menopausal women reported with calcification on digital panoramic radiographs with a prevalence of 11% (16). Maria Priscilla David et al in her retrospective study out of 84 panoramic radiographs 25% showed the presence of CAC (3). Hence the range of the prevalence of CAC of the reported studies ranged from 5.94-25% which is similar to the prevalence of our study.

The wide range in prevalence may be attributed to lifestyle difference of subjects including dietary habit, health consciousness, and regional variations.

In the present study mean age of the postmenopausal women with periodontitis is 53.3 years which was in accordance with the studies done by L.crater et al[16], Tamura et al (12), Sisman et al with a mean age of 40.1-62.2 years which is coinciding with the mean age of the present study (17).

In our study mean age of postmenopausal women with periodontitis and CACs was 50.47 and postmenopausal women with periodontitis and without CACs were 51.88 which is in variance with a study done by Maria Priscilla David et al[19] where the mean age of subjects with CAC was 61.57 and without CACs was 54.95.This could be due to variation in sample size and regional variations. In the present study mean and standard deviation of PRI in postmenopausal women with periodontitis and CACs was found to be significantly higher (28±7) than the PRI of postmenopausal women with periodontitis and without CACs (22±7) with a p-value of 0.0004.This was in accordance with the previous study done by Maria Priscilla David et al (3) with a mean and standard deviation of 28.3±11.88, 22.06± 9.9 respectively. The subjects with more PRI i.e. alveolar percentage bone loss are more prone to develop CAC.

In our present study out of 19 subjects with CAC, 13 (68.4%) were bilateral calcifications and 6 were unilateral with 2(10.5%) on the left side and 4 (21%) on the right side (Table 3). Our study was in accordance with Yildiray Sisman et al (17) and Taheri et al (16), where 31 (62%) of the CACs were located on the right side and 19 (38%) were located on the left side in the former report and 40.9% of CACs were on right side and 31.8% showed on left side in latter report.

In our present study, 19 individuals who were confirmed with CAC through panoramic radiography agreed for evaluation with carotid Doppler Ultrasound which is non-invasive and non-ionizing modality. All these patients were asymptomatic at the time of the study. All these 19 subjects confirmed to have atherosclerotic plaques in the carotid Doppler Ultrasound. In previously reported studies by Bayram et al (18) Ravon et al (19) Friedlander et al (20), it was found that 35%, 34.9%, 23% of the panoramic detected CAC were confirmed with color Doppler ultrasonography.

When subjected to ultrasound, 7 (36.8%) were confirmed to have calcified atheromas unilaterally and 12 (63.12%) were confirmed to have calcified atheromas bilaterally (Table-5). And the values obtained for sensitivity was 85.71% and for specificity was 100% for determining the inclusion of digital panoramic radiograph as a detecting tool for carotid artery calcifications (Table-6).

In our present study, the PRI of postmenopausal women showing carotid artery calcification was 28±7mm and PRI of postmenopausal women without carotid artery calcification was found to be 22±7mm. The difference between these two mean values was analyzed using student t-test thus showing strong statistically significant correlation ($p \leq 0.0004$) between the PRI index with carotid artery calcification and without carotid artery calcification (Table 7)

The results obtained were in line with the study conducted by Maria Priscilla David et al (3) where the mean bone loss in subjects with absent carotid artery calcification (CAC) was 22.06 mm and in subjects with present CAC was 28.30 mm. Higher mean bone loss was recorded in samples with the presence of CAC compared to samples with the absence of CAC ($p<0.05$).

Poorly maintained oral health manifesting as severe tooth loss due to severe periodontal disease may be a positive predictor of the cerebrovascular and cerebral infarct. Some factors that are common risk factors and thus link the association between periodontal disease and atherosclerosis are smoking, obesity, and diabetes. This association may reflect a propensity to develop an enhanced inflammatory response to intrinsic (age, sex, genes) or extrinsic stimuli (diet, smoking, etc) resulting in insidious development of an inflammatory focus in the oral cavity that may further may potentiate the atherosclerotic process through activation of humoral and cell-mediated inflammatory pathways characterised by increase C-reactive protein, interleukins , TNF – alpha, prostaglandins etc. The presence of periodontal infection may lead to brief episodes of bacteraemia with inoculation of atherosclerotic plaques by periodontal pathogens such as Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans, and Bacteroides forsythus which can aggravate these pathological inflammatory process (11, 21, 22).[27] Periodontal pathogens like Porphyromonas gingivalis have been demonstrated in atherosclerotic plaques(23-25).

The present study, emphasizes the role of the Oral Physician and radiologist in providing the valuable adjuvant information by evaluating the digital panoramic radiograph to detect CAC and thus further directing the patients to a physician when a suspected calcification is identified on panoramic radiographs. Therefore, this study proves that panoramic radiography might be used as a screening tool for the identification of carotid calcifications but further studies to assess the reliability of panoramic radiography in the identification of CAC should be recommended.

All the patients in our study who showed CCA in OPG were referred to a physician for further evaluation and management regarding the presence and extent of the disease. Patients were motivated for dietary & lifestyle modifications as an extension of the role of Oral Physician for the control of risk factors and thereby to retard and possibly reverse the atherogenic process and prevent future risk of cerebrovascular accidents.

IV. Tables and figures

Table 1: Demographic distribution of the study:

S.no		Total	Mean±SD
1	Total no. of patients	112757	233.2 ±67
2	Males	56595	115.5 ±29.9
3	Males>45Yrs	6124	14.2 ±8.2
4	Females	53956	111±29
5	Females>45Yrs	5818	10.2 ±7.6

Table 2: Depiction of post-menopausal female patients with periodontitis:

S. No		Total	Mean ± SD
	Menopause	978	1.93±2
	Periodontitis	250	0.49±0.89

Table 3: Distribution of menopausal women Age and PRI index:

AGE(years)	PRI INDEX		
	Total	Range (mm)	MEAN±SD
46-55	205	17.28-52.9	28.1±9.2
56-65	41	19.4-42.5	25.5±6.3
66-75	4	21.9-42.5	28.6±9.6

Table 4: Distribution of carotid artery calcifications and their occurrence in OPG accordingly:

Patients with positive CAC	GROUP	
	UNILATERAL	BILATERAL
TOTAL (19)	6 (31.57%)	13 (68.42%)

Table 5: Distribution of carotid artery calcifications and their occurrence in USG accordingly:

s with positive Carotid artery calcifications	GROUP	
	ILATERALLY PRESENT	LATERALLY PRESENT
TOTAL(19)	7(36.8%)	12(63.12%)

Table-6: Sensitivity, Specificity, Positive predictive value and Negative predictive values of Carotid artery calcifications occurrence in OPG & USG.

Measurements	Carotid artery calcifications
Sensitivity (%)	85.71
Specificity (%)	100
Positive predictive value (%)	100
Negative predictive value (%)	92.31

Table 7: Distribution of carotid artery calcifications and PRI index accordingly:

	OPG & USG CALCIFICATIONS	Age MEAN±SD p-value(0.6)	PRI index ıge in mm	 MEAN±SD p-value (0.0004)
POSITIVE	19	50.47±4.8	20.45-42.52	28±7
NEGATIVE	231	51.88±5.2	17.28-52.9	22±7

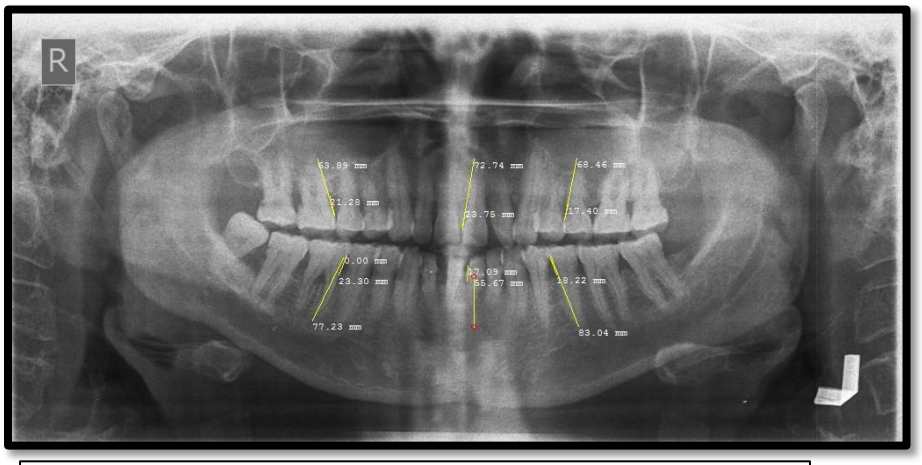

Figure 1: Digital panoramic image depicting PRI calibrations.

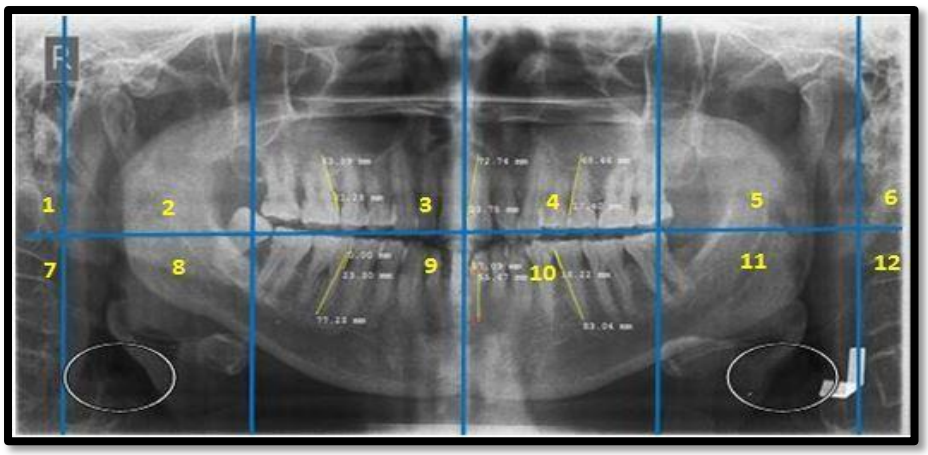

Figure 2: Digital panoramic image showing bilateral carotid artery calcifications in 8 & 11 boxes.

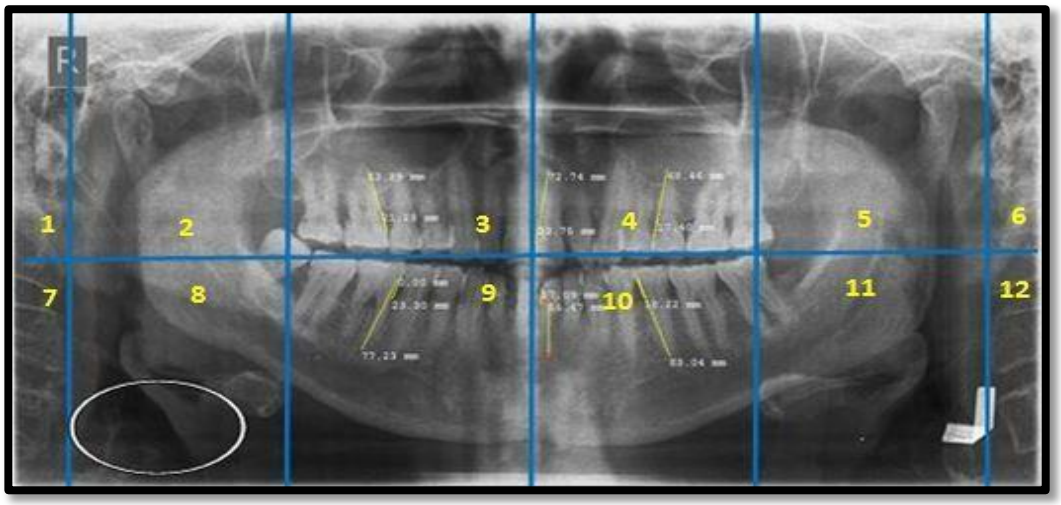

Figure 3: Digital panoramic image showing unilateral carotid artery calcifications in box 8

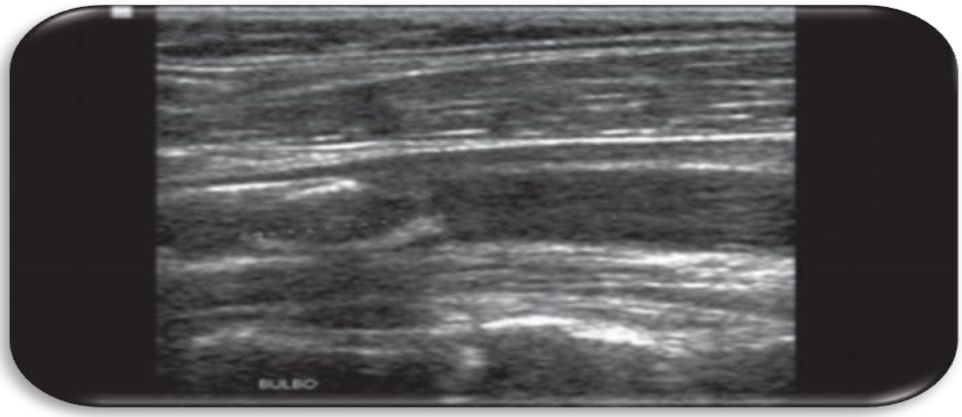

Figure 4: Ultrasonograohy depicting carotid artery calcification

V. Conclusion

From our study, it as elucidated that there was the statistically significant difference between the PRI of the postmenopausal women having periodontitis with CACs and post-menopausal women were having periodontitis without CACs, thus showing a strong correlation between periodontitis and CACs in post-menopausal women on digital panoramic radiography in East Godavari population. These simple and cost-effective measures help to implement preventive strategies in life-threatening diseases like cardiovascular and cerebrovascular disorders. However further studies with larger sample size are suggested to substantiate our findings.

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