
Calcified carotid atherosclerotic plaque in panoramic radiographs in patients with Diabetes mellitus- A Retrospective Study

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Abstract: Atherosclerosis is characterized by thickening and loss of elasticity of the arterial walls, associated with the presence of atheromatous plaques. It is associated with diabetes mellitus and leads to increased risk of stroke. The aim of this study is to determine the prevalence of atherosclerotic plaques in panoramic radiograph in patients with diabetes mellitus. A retrospective study was carried out in diabetic patients who took panoramic radiographs for routine dental examination visiting Radiology department. The data were obtained from analysing 86000 patients records between June 2019-March 2020. The data comprised of 220 diabetic patients who visited Radiology department. The collected data were entered into Excel sheet and subjected to statistical analysis using SPSS software. A chi square test was done between variables. Results showed that prevalence of atherosclerotic plaque on panoramic radiographs in patients with diabetes mellitus was found to be 34.09%. Out of 34.09%, 61.11% had unilateral atherosclerotic plaque and 38.89% had bilateral atherosclerotic plaque. Statistically significant association was found between age and presence of atherosclerotic plaque (p-value:0.014). The present study concludes that presence of atherosclerotic plaque was found highly in female diabetic patients and patients under 40-60 age group.

Keywords: Atherosclerotic plaque, Carotid, Diabetes mellitus, Panoramic radiographs.

INTRODUCTION

Atheromas are calcified plaques composed of lipids and fibrous tissue, which are deposited on the walls of blood vessels leading to atherosclerosis. Atherosclerosis is a chronic inflammatory disease of a multifactorial nature, characterized by thickening and loss of elasticity of the arterial walls, associated with the presence of atheromas. When atherosclerosis affects the arteries that supply the brain, the carotids, strokes can be triggered, and when it affects arteries that supply the heart, the coronary arteries, there is a possibility of myocardial infarction, events that result in the death of the person (Zhdanov and Sternby, 2004). There are various factors which predisposes the development of atherosclerosis, such as diabetes mellitus, obesity, arterial hypertension, smoking, alcoholism, inadequate diet and eating habits, periodontitis, chronic renal disease, menopause, etc. The atherosclerotic process begins in childhood and the clinical manifestations occur in adult life, particularly after 45 years of age (Fatahzadeh and Glick, 2006).

Cerebrovascular accidents or strokes are the third most common cause of morbidity and mortality worldwide. The main cause of cerebrovascular accidents is rupture of atherosclerotic plaques present in carotid arteries. The carotid bifurcation is at the highest risk of atherosclerosis. At carotid arterial bifurcation, flow velocity and shear stress are reduced, and flow departs in a laminar, unidirectional pattern. Fatty streaks located at bifurcations may progress to smooth muscle-rich fibrous plaques that are prone to calcification (Yoon *et al.*, 2008).

Diabetes mellitus is currently the fastest growing debilitating disease in the world. Diabetes mellitus increases the risk of cerebrovascular accidents leading to death (Almog *et al.*, 2000). Diabetic people are at heightened risk of stroke because hyperglycemia, hyperlipidemia, and hypertension often associated with the disorder have been implicated as the cause of atherosclerosis of the carotid artery. Besides the well-recognized microvascular complications of diabetes, there is increased incidence of macrovascular complications like diseases of coronary arteries, peripheral arteries, and carotid vessels. The risk of stroke is increased by 150-400% in patients with diabetes (Beckman, Creager and Libby, 2002).

In recent years, a number of publications have described the detection of calcifications in the region of carotid bifurcation on panoramic radiographs. Previous studies have reported a prevalence rate of 2-11% for calcified carotid artery atheromatous plaques (CCAP) on panoramic radiographs in general dental patient population (Roldán-Chicano *et al.*, 2006)

Several researchers have demonstrated the presence of CACs on dental panoramic radiographs, which might be a useful indicator to identify asymptomatic dental patients who may benefit from further examination by medical professionals (Hubar, 1999; Almog *et al.*, 2002; London *et al.*, 2004). Despite the number of publications about the presence of CACs on the panoramic radiography among various populations, there has been no detailed information about this condition in diabetic patients. Hence, we evaluated the presence of carotid artery calcifications (CACs) detected on dental panoramic radiographs among a group of diabetic patients attending university dental hospitals.

Previously our team had conducted numerous case studies (Choudhury *et al.*, 2015) (Misra *et al.*, 2015) (Dharman and Muthukrishnan, 2016) (Muthukrishnan, Bijai Kumar and Ramalingam, 2016) (Muthukrishnan and Bijai Kumar, 2017) and systematic reviews (Venugopal and Uma Maheswari, 2016) (Chaitanya *et al.*, 2017) (Chaitanya *et al.*, 2018) (Maheswari *et al.*, 2018) and questionnaire based studies (Subashri and Maheswari, 2016) (Muthukrishnan and Warnakulasuriya, 2018) and international validation study (Steele *et al.*, 2015) and radiographic studies (Rohini and Kumar, 2017) (Patil *et al.*, 2018) (Subha and Arvind, 2019) over the past 5 years. Despite the number of publications about the presence of CACs on the panoramic radiography among various populations, there has been no detailed information about this condition in diabetic patients. Hence, the aim was to evaluate the presence of carotid artery calcifications (CACs) detected on dental panoramic radiographs among a group of diabetic patients attending an University dental hospitals. Our team has rich experience in research and we have collaborated with numerous authors over various topics in the past decade (Deogade, Gupta and Ariga, 2018; Ezhilarasan, 2018; Ezhilarasan, Sokal and Najimi, 2018; Jeevanandan and Govindaraju, 2018; J *et al.*, 2018; Menon *et al.*, 2018; Prabakar *et al.*, 2018; Rajeshkumar *et al.*, 2018, 2019; Vishnu Prasad *et al.*, 2018; Wahab *et al.*, 2018; Dua *et al.*, 2019; Duraisamy *et al.*, 2019; Ezhilarasan, Apoorva and Ashok Vardhan, 2019; Gheena and Ezhilarasan, 2019; Malli Sureshbabu *et al.*, 2019; Mehta *et al.*, 2019; Panchal, Jeevanandan and Subramanian, 2019; Rajendran *et al.*, 2019; Ramakrishnan, Dhanalakshmi and Subramanian, 2019; Sharma *et al.*, 2019; Varghese, Ramesh and Veeraiyan, 2019; Gomathi *et al.*, 2020; Samuel, Acharya and Rao, 2020)

MATERIALS AND METHODS

Study design

Retrospective study

Study population

A retrospective study was carried out among diabetic patients reporting to the Radiology Department. The study was conducted between June 2019-March 2020. The study population consisted of diabetic patients who took panoramic radiographs for routine dental examination. The inclusion criteria includes: diabetic patients with panoramic radiographs, random blood sugar level of patients and duration of diabetes. The exclusion criteria includes: diabetic patients without OPG, incomplete data.

Ethical approval

Ethical approval was obtained from the Institutional Ethical Committee and Scientific Review Board (SRB) of Saveetha Dental College. SDC/SIHEC/2020/DIASDATA/0619-0320.

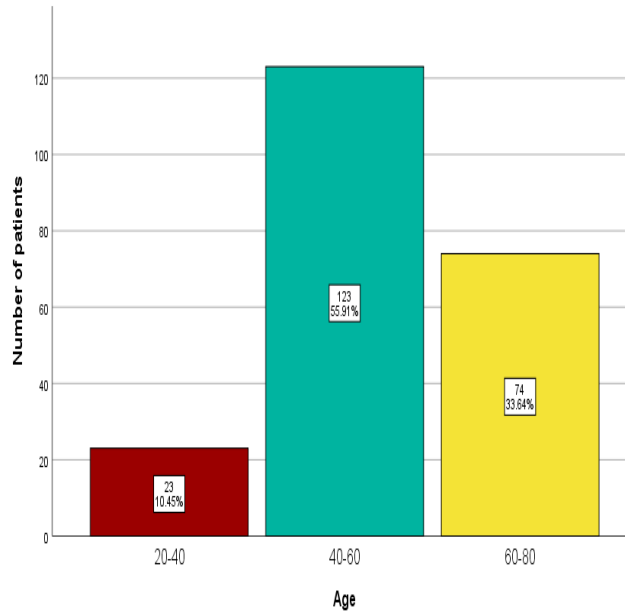
Data collection

The data were collected by analyzing the records of 86000 patients between June 2019-March 2020. The data comprised 220 diabetic patients who visited Radiology department and underwent dental panoramic radiographs for the diagnosis of dental lesions were selected for this study. The data includes patient's details, duration of diabetes, random blood sugar level values and presence or absence of atherosclerotic plaques which are either unilateral or bilateral were recorded. The data were analysed by 2 reviewers-the primary researcher and department faculty.

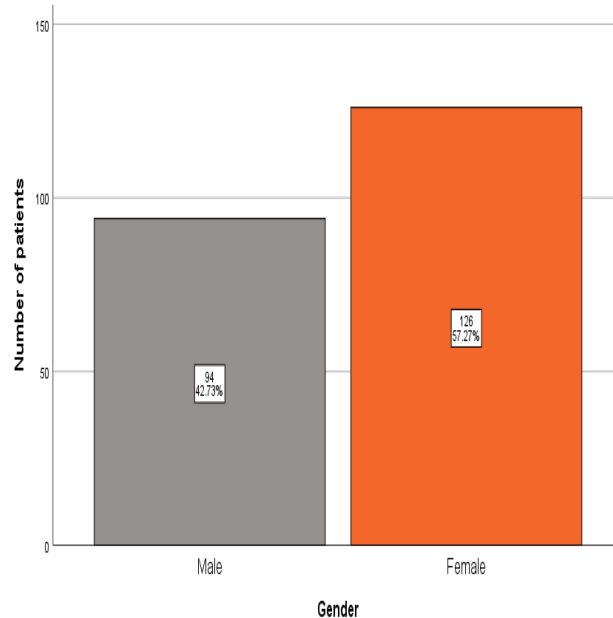
Data analysis

The collected data were entered in Excel sheet and subjected to statistical analysis using SPSS software. A chi square test was done. The independent variables present in this study were age and gender. The dependent variables were duration of diabetes, random blood sugar level and atherosclerotic plaque. The type of analysis used for this study was association.

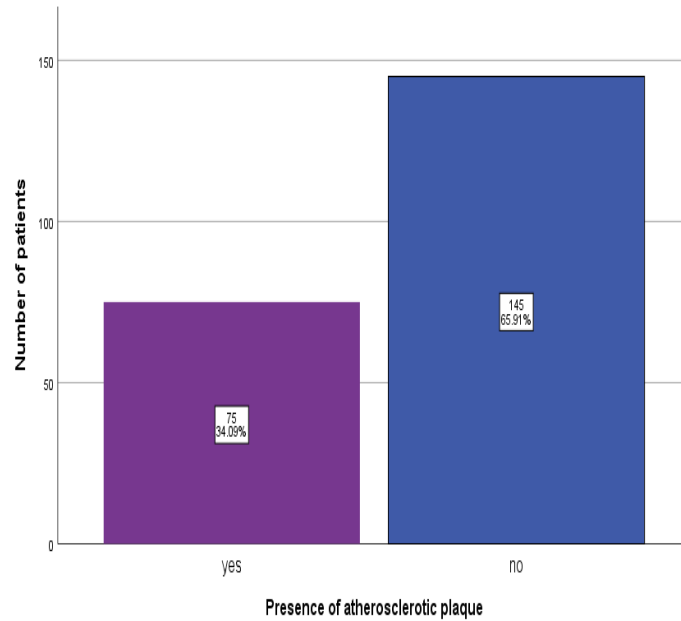
RESULTS AND DISCUSSION



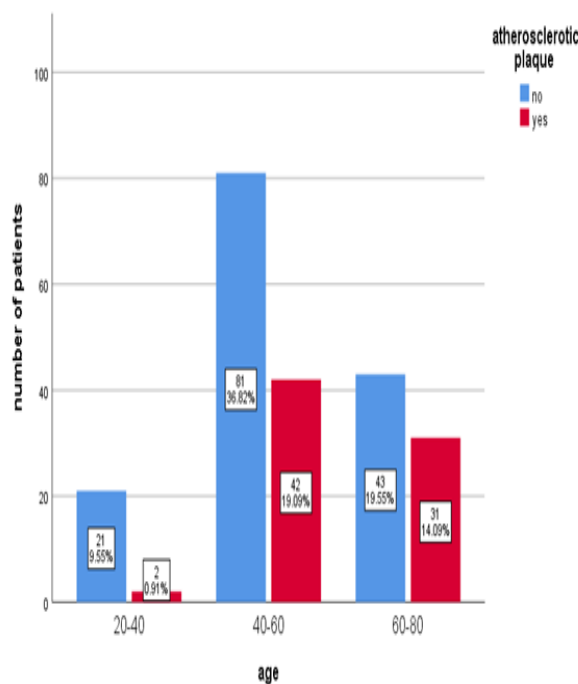
Graph 1: Bar chart showing the distribution of study population based on age. X-axis represents the age group and Y-axis represents the number of patients. It shows that most number of diabetic patients were seen in the 40-60 age group (green) followed by 60-80 age group (yellow).



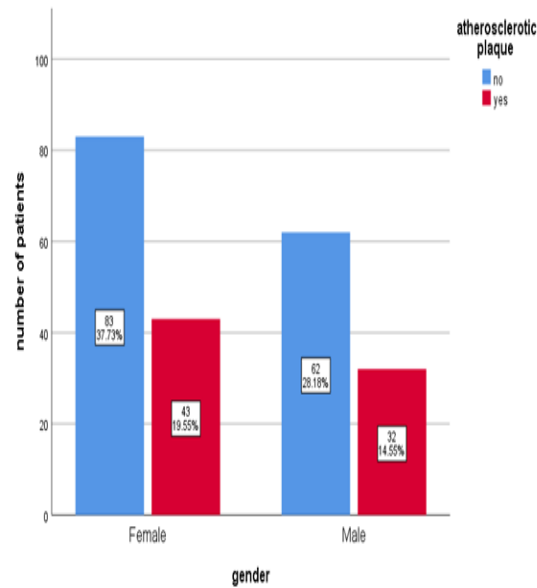
Graph 2: Bar chart showing the distribution of study population based on gender. It shows that the majority of female patients (orange) are reported with diabetes mellitus and undertook panoramic radiographs when compared to male patients (grey).



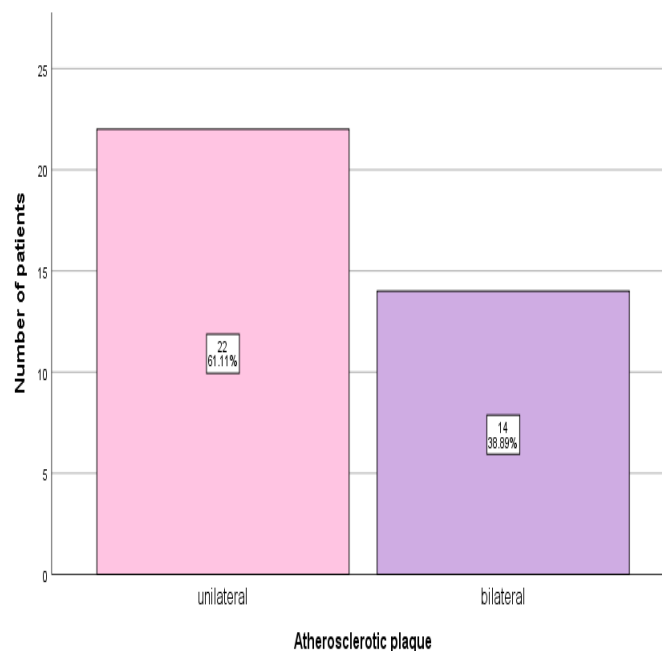
Graph 3: Bar chart showing the distribution of presence of atherosclerotic plaque among study population. X axis represents the presence of atherosclerotic plaque and Y axis represents number of patients. We found that about 34.09% diabetic patients had presence of atherosclerotic plaque (purple) while 65.91% diabetic patients had absence of atherosclerotic plaque (dark blue) in panoramic radiographs.



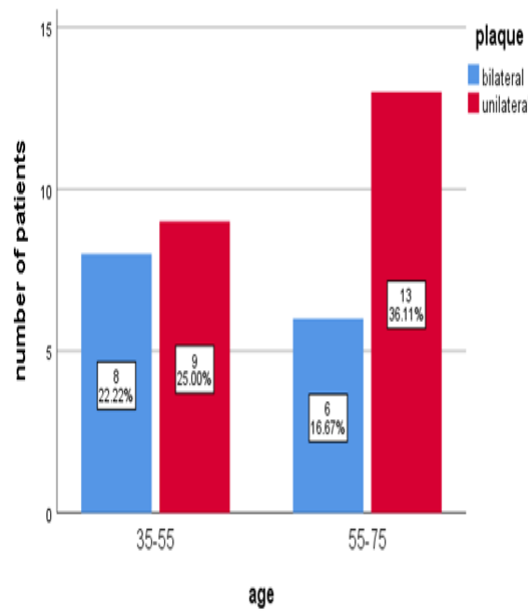
Graph 4: This graph represents the association between age group and presence of atherosclerotic plaque. X axis represents age group and Y axis represents number of diabetic patients. We found that a higher prevalence of atherosclerotic plaque (red) was seen in the 40-60 age group [19.09%]. Association between age group and presence of atherosclerotic plaque was done using Chi-square test ($p < 0.05$) and was found to be statistically significant.



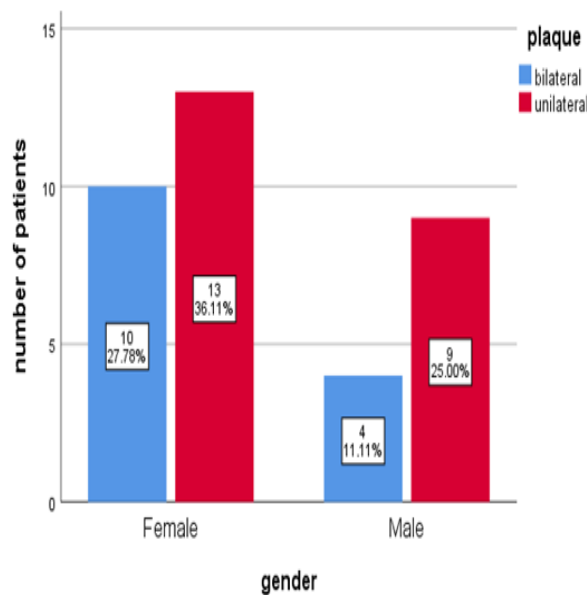
Graph 5: This graph represents the association between gender and presence of atherosclerotic plaque. X axis represents gender and Y axis represents number of diabetic patients. We found female diabetic patients [19.53%] had higher prevalence of atherosclerotic plaque (red) when compared to male diabetic patients [14.55%]. Association between gender and presence of atherosclerotic plaque was done using Chi-square test ($p > 0.05$) and was found to be statistically not significant.



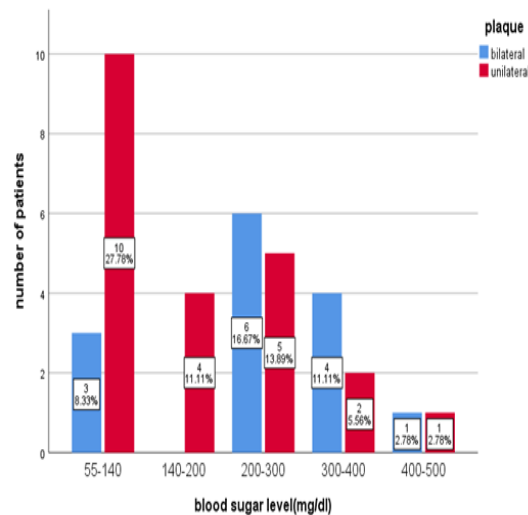
Graph 6: Bar chart showing the unilateral and bilateral distribution of atherosclerotic plaque among study population. X axis represents the atherosclerotic plaque and Y axis represents number of patients. We found that more number of diabetic patients had unilateral atherosclerotic plaque (pink) [61.11] when compared to bilateral atherosclerotic plaque (violet) [38.89%].



Graph 7: This graph represents the association between age group and atherosclerotic plaque. X axis represents age group and Y axis represents number of diabetic patients. We found that the majority of patients with unilateral atherosclerotic plaque (red) were seen in the 55-75 age group. Association between age group and atherosclerotic plaque was done using Chi-square test ($p > 0.05$) and was found to be statistically not significant.



Graph 8: This graph represents the association between gender and atherosclerotic plaque. X axis represents gender and Y axis represents number of diabetic patients. It shows that female diabetic patients had high prevalence rate in unilateral atherosclerotic plaque (red) [36.11%] when compared to bilateral atherosclerotic plaque (blue) [27.78%]. Association between gender and atherosclerotic plaque was done using Chi-square test ($p > 0.05$) and was found to be statistically not significant.



Graph 9: This graph represents the association between blood sugar level and atherosclerotic plaque. X axis represents blood sugar level and Y axis represents number of diabetic patients. It shows higher incidence of unilateral atherosclerotic plaque (red) were seen among patients with blood sugar level ranging 55-140mg/dl [27.78%]. Association between blood sugar level and atherosclerotic plaque was done using Chi-square test ($p > 0.05$) and was found to be statistically not significant.

The study population consisted of 220 diabetic patients who undertook panoramic radiographs for routine dental examination. Among 220 diabetic patients, 55.91% were belongs to the age group of 40-60, 33.64% were 60-80 age group and 10.45% were 20-40 age group (graph 1). Out of 220 patients, 42.73% were males and 57.27% were females (graph 2)

A total of 220 panoramic radiographs of diabetic patients were analysed. Of which, 75 panoramic radiographs of subjects were detected the presence of atherosclerotic plaque [34.09%] (graph 3). The higher incidence of atherosclerotic plaque was seen in the 40-60 age group [19.09%] followed by 60-80 [14.09%]. The least incidence was seen in the 20-40 age group [0.92%]. Association between age and presence of atherosclerotic plaque was found to be statistically significant [$p < 0.05$] (graph 4). Female diabetic patients [19.53%] were highly present with atherosclerotic plaque in panoramic radiographs when compared to male diabetic patients [14.55%]. Association between gender and presence of atherosclerotic was found to be statistically insignificant [$p > 0.05$] (Graph 5).

The evaluation of the CCAPs occurrence revealed that unilateral and bilateral atherosclerotic plaque were present in the subjects. Unilateral atherosclerotic plaque [61.11%] were in higher numbers in panoramic radiographs of diabetic patients (graph 6). Higher prevalence of unilateral atherosclerotic plaque were seen in the 55-75 age group [36.11%] while bilateral atherosclerotic plaque were seen in the 35-55 age group [16.67%]. The association between age group and atherosclerotic plaque showed that chi square test p -value > 0.05 , statistically insignificant (graph 7). More number of female diabetic patients [36.11%] had unilateral atherosclerotic plaque when compared to male diabetic patients [27.78%]. The association between gender and atherosclerotic plaque showed chi square test p -value > 0.05 , statistically significant (graph 8). Incidence of unilateral atherosclerotic plaque were seen among patients with blood sugar level ranging 55-140 mg/dl [27.78%] while bilateral atherosclerotic plaque were seen among patients with blood sugar level ranging 200-300mg/dl [16.67%] which was found to be statistically insignificant (Graph 9).

The prevalence of CCAP on panoramic radiographs of patients with diabetes mellitus was found to be 33.9% of which 61.11% had unilateral atherosclerotic plaque and 38.89% had bilateral atherosclerotic plaque. These results were compared with other previous studies. In 2000, Friedlander *et al.* (Friedlander and Maeder, 2000) reported 20.4% prevalence of CCAPs were reported in panoramic radiographs of patients with diabetes mellitus which is dissimilar to our present study. A study by Tofangchiha *et al.* (Tofangchiha *et al.*, 2011) involving 158 patients with diabetes mellitus type 2 showed that the frequency of calcified carotid atheromas on panoramic radiographs is higher in diabetic patients than in normal individuals. A study conducted by Yoon *et al.* (Yoon *et al.*, 2008) and Yusuf Atalay *et al.* (Atalay *et al.*, 2015) showed 62.3% and 63.44% accuracy for the detection of CCA using panoramic radiographs. The prevalence rate was higher than our present study. In the before mentioned study, Thirty-eight (82.6%) of the 46 diabetic patients diagnosed with unilateral calcifications, while 8 (17.4%) of them had bilateral calcifications (Tofangchiha *et al.*, 2011).

Increasing age is a predisposing factor for progression of atherosclerosis. In our study, we found that the highest prevalence of CCAP was in the age group of 40-60 years. A total of 42 patients out of 123 showed the presence

of CCAP in the age group 40-60 years. A study conducted by Neha Khambete et al (Khambete and Kumar, 2015) and Beckstrom (Beckstrom *et al.*, 2007) reported that 70-79 age group were highly present with atherosclerotic plaque.

In this study, we found that the highest prevalence of CCAP was seen in female patients. Previous studies conducted by Bayram *et al* (Bayram *et al.*, 2006) and Kumagai *et al* (Kumagai *et al.*, 2007) which consistently showed that the prevalence of CCAP was seen in females more than males.

Limitations

The limitations of this present study can be improved by increasing the sample size and having multi centre study. In the future, with the knowledge about detection of atherosclerotic plaque in panoramic radiographs which will be a useful indicator for asymptomatic patients. Our institution is passionate about high quality evidence based research and has excelled in various fields ((Pc, Marimuthu and Devadoss, 2018; Ramesh *et al.*, 2018; Ezhilarasan, Apoorva and Ashok Vardhan, 2019; Ramadurai *et al.*, 2019; Sridharan *et al.*, 2019; Vijayashree Priyadharsini, 2019; Mathew *et al.*, 2020)

CONCLUSION

Within the limits of this study, we concluded that prevalence of CCAPs on panoramic radiographs of patients with diabetes mellitus was significantly higher in female patients and 40-60 age groups. Statistically significant association was found between age and presence of atherosclerotic plaque.

ACKNOWLEDGEMENT

I sincerely express my gratitude and acknowledgement to the Director, Dean and management for their support and also thank the Research and IT department of Saveetha dental college for their affable assistance in acquiring the data.

REFERENCES

1. Almog, D. M. et al. (2000) 'Unrecognized carotid artery stenosis discovered by calcifications on a panoramic radiograph', *Journal of the American Dental Association*, 131(11), pp. 1593–1597.
2. Almog, D. M. et al. (2002) 'Correlating carotid artery stenosis detected by panoramic radiography with clinically relevant carotid artery stenosis determined by duplex ultrasound', *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics*, 94(6), pp. 768–773.
3. Atalay, Y. et al. (2015) 'Evaluation of calcified carotid atheroma on panoramic radiographs and Doppler ultrasonography in an older population', *Clinical interventions in aging*, 10, pp. 1121–1129.
4. Bayram, B. et al. (2006) 'Digital panoramic radiography: a reliable method to diagnose carotid artery atheromas?', *Dento maxillo facial radiology*, 35(4), pp. 266–270.
5. Beckman, J. A., Creager, M. A. and Libby, P. (2002) 'Diabetes and atherosclerosis: epidemiology, pathophysiology, and management', *JAMA: the journal of the American Medical Association*, 287(19), pp. 2570–2581.
6. Beckstrom, B. W. et al. (2007) 'Correlation between carotid area calcifications and periodontitis: a retrospective study of digital panoramic radiographic findings in pretreatment cancer patients', *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics*, 103(3), pp. 359–366.
7. Chaitanya, N. C. et al. (2017) 'Role of Vitamin E and Vitamin A in Oral Mucositis Induced by Cancer Chemo/Radiotherapy- A Meta-analysis', *Journal of clinical and diagnostic research: JCDR*, 11(5), pp. ZE06–ZE09.
8. Chaitanya, N. C. et al. (2018) 'An Insight and Update on the Analgesic Properties of Vitamin C', *Journal of pharmacy & bioallied sciences*, 10(3), pp. 119–125.
9. Choudhury, P. et al. (2015) 'Vanishing roots: first case report of idiopathic multiple cervico-apical external root resorption', *Journal of clinical and diagnostic research: JCDR*, 9(3), pp. ZD17–9.
10. Deogade, S., Gupta, P. and Ariga, P. (2018) 'Effect of monopoly-coating agent on the surface roughness of a tissue conditioner subjected to cleansing and disinfection: A Contact Profilometric In vitro study', *Contemporary Clinical Dentistry*, p. 122. doi: 10.4103/ccd.ccd_112_18.
11. Dharmar, S. and Muthukrishnan, A. (2016) 'Oral mucous membrane pemphigoid - Two case reports with varied clinical presentation', *Journal of Indian Society of Periodontology*, 20(6), pp. 630–634.
12. Dua, K. et al. (2019) 'The potential of siRNA based drug delivery in respiratory disorders: Recent advances and progress', *Drug development research*, 80(6), pp. 714–730.
13. Duraisamy, R. et al. (2019) 'Compatibility of Nonoriginal Abutments With Implants: Evaluation of Microgap at the Implant-Abutment Interface, With Original and Nonoriginal Abutments', *Implant dentistry*, 28(3), pp. 289–295.
14. Ezhilarasan, D. (2018) 'Oxidative stress is bane in chronic liver diseases: Clinical and experimental perspective', *Arab journal of gastroenterology: the official publication of the Pan-Arab Association of*

- Gastroenterology, 19(2), pp. 56–64.
15. Ezhilarasan, D., Apoorva, V. S. and Ashok Vardhan, N. (2019) 'Syzygium cumini extract induced reactive oxygen species-mediated apoptosis in human oral squamous carcinoma cells', *Journal of oral pathology & medicine: official publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology*, 48(2), pp. 115–121.
 16. Ezhilarasan, D., Sokal, E. and Najimi, M. (2018) 'Hepatic fibrosis: It is time to go with hepatic stellate cell-specific therapeutic targets', *Hepatobiliary & pancreatic diseases international: HBPD INT*, 17(3), pp. 192–197.
 17. Fatahzadeh, M. and Glick, M. (2006) 'Stroke: epidemiology, classification, risk factors, complications, diagnosis, prevention, and medical and dental management', *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics*, 102(2), pp. 180–191.
 18. Friedlander, A. H. and Maeder, L. A. (2000) 'The prevalence of calcified carotid artery atheromas on the panoramic radiographs of patients with type 2 diabetes mellitus', *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics*, 89(4), pp. 420–424.
 19. Gheena, S. and Ezhilarasan, D. (2019) 'Syringic acid triggers reactive oxygen species-mediated cytotoxicity in HepG2 cells', *Human & experimental toxicology*, 38(6), pp. 694–702.
 20. Gomathi, A. C. et al. (2020) 'Anticancer activity of silver nanoparticles synthesized using aqueous fruit shell extract of Tamarindus indica on MCF-7 human breast cancer cell line', *Journal of Drug Delivery Science and Technology*, p. 101376. doi: 10.1016/j.jddst.2019.101376.
 21. Hubar, J. S. (1999) 'Carotid artery calcification in the black population: a retrospective study on panoramic radiographs', *Dento maxillo facial radiology*, 28(6), pp. 348–350.
 22. Jeevanandan, G. and Govindaraju, L. (2018) 'Clinical comparison of Kedo-S paediatric rotary files vs manual instrumentation for root canal preparation in primary molars: a double blinded randomised clinical trial', *European Archives of Paediatric Dentistry*, pp. 273–278. doi: 10.1007/s40368-018-0356-6.
 23. J, P. C. et al. (2018) 'Prevalence and measurement of anterior loop of the mandibular canal using CBCT: A cross sectional study', *Clinical implant dentistry and related research*, 20(4), pp. 531–534.
 24. Khambete, N. and Kumar, R. (2015) 'Calcified carotid atherosclerotic plaques on digital panoramic radiographs in patients with Type II diabetes mellitus: A case control study', *Journal of Indian Academy of Oral Medicine and Radiology*, 27(1), p. 42.
 25. Kumagai, M. et al. (2007) 'Carotid artery calcification seen on panoramic dental radiographs in the Asian population in Japan', *Dento maxillo facial radiology*, 36(2), pp. 92–96.
 26. London, G. M. et al. (2004) 'Arterial calcifications and bone histomorphometry in end-stage renal disease', *Journal of the American Society of Nephrology: JASN*, 15(7), pp. 1943–1951.
 27. Maheswari, T. N. U. et al. (2018) 'Salivary micro RNA as a potential biomarker in oral potentially malignant disorders: A systematic review', *Ci ji yi xue za zhi = Tzu-chi medical journal*, 30(2), pp. 55–60.
 28. Malli Sureshbabu, N. et al. (2019) 'Concentrated Growth Factors as an Ingenious Biomaterial in Regeneration of Bony Defects after Periapical Surgery: A Report of Two Cases', *Case reports in dentistry*, 2019, p. 7046203.
 29. Mathew, M. G. et al. (2020) 'Evaluation of adhesion of Streptococcus mutans, plaque accumulation on zirconia and stainless steel crowns, and surrounding gingival inflammation in primary ...', *Clinical oral investigations*. Available at: <https://link.springer.com/article/10.1007/s00784-020-03204-9>.
 30. Mehta, M. et al. (2019) 'Oligonucleotide therapy: An emerging focus area for drug delivery in chronic inflammatory respiratory diseases', *Chemico-biological interactions*, 308, pp. 206–215.
 31. Menon, S. et al. (2018) 'Selenium nanoparticles: A potent chemotherapeutic agent and an elucidation of its mechanism', *Colloids and Surfaces B: Biointerfaces*, pp. 280–292. doi: 10.1016/j.colsurfb.2018.06.006.
 32. Misra, S. R. et al. (2015) 'Metastatic hepatocellular carcinoma in the maxilla and mandible, an extremely rare presentation', *Contemporary clinical dentistry*, 6(Suppl 1), pp. S117–21.
 33. Muthukrishnan, A. and Bijai Kumar, L. (2017) 'Actinic cheilosis: early intervention prevents malignant transformation', *BMJ case reports*, 2017. doi: 10.1136/bcr-2016-218654.
 34. Muthukrishnan, A., Bijai Kumar, L. and Ramalingam, G. (2016) 'Medication-related osteonecrosis of the jaw: a dentist's nightmare', *BMJ case reports*, 2016. doi: 10.1136/bcr-2016-214626.
 35. Muthukrishnan, A. and Warnakulasuriya, S. (2018) 'Oral health consequences of smokeless tobacco use', *The Indian journal of medical research*, 148(1), pp. 35–40.
 36. Panchal, V., Jeevanandan, G. and Subramanian, E. M. G. (2019) 'Comparison of post-operative pain after root canal instrumentation with hand K-files, H-files and rotary Kedo-S files in primary teeth: a randomised clinical trial', *European archives of paediatric dentistry: official journal of the European Academy of Paediatric Dentistry*, 20(5), pp. 467–472.
 37. Patil, S. R. et al. (2018) 'Three-Rooted Mandibular First Molars in a Saudi Arabian Population: A CBCT Study', *Pesquisa brasileira em odontopediatria e clinica integrada*, 18(1), p. 4133.
 38. Pc, J., Marimuthu, T. and Devadoss, P. (2018) 'Prevalence and measurement of anterior loop of the

- mandibular canal using CBCT: A cross sectional study', *Clinical implant dentistry and related research*. Available at: <https://europepmc.org/article/med/29624863>.
39. Prabakar, J. et al. (2018) 'Comparative Evaluation of Retention, Cariostatic Effect and Discoloration of Conventional and Hydrophilic Sealants - A Single Blinded Randomized Split Mouth Clinical Trial', *Contemporary clinical dentistry*, 9(Suppl 2), pp. S233–S239.
 40. Rajendran, R. et al. (2019) 'Comparative Evaluation of Remineralizing Potential of a Paste Containing Bioactive Glass and a Topical Cream Containing Casein Phosphopeptide-Amorphous Calcium Phosphate: An in Vitro Study', *Pesquisa Brasileira em Odontopediatria e Clínica Integrada*, pp. 1–10. doi: 10.4034/pboci.2019.191.61.
 41. Rajeshkumar, S. et al. (2018) 'Biosynthesis of zinc oxide nanoparticles using *Mangifera indica* leaves and evaluation of their antioxidant and cytotoxic properties in lung cancer (A549) cells', *Enzyme and microbial technology*, 117, pp. 91–95.
 42. Rajeshkumar, S. et al. (2019) 'Antibacterial and antioxidant potential of biosynthesized copper nanoparticles mediated through *Cissus arnotiana* plant extract', *Journal of photochemistry and photobiology. B, Biology*, 197, p. 111531.
 43. Ramadurai, N. et al. (2019) 'Effectiveness of 2% Articaine as an anesthetic agent in children: randomized controlled trial', *Clinical oral investigations*, 23(9), pp. 3543–3550.
 44. Ramakrishnan, M., Dhanalakshmi, R. and Subramanian, E. M. G. (2019) 'Survival rate of different fixed posterior space maintainers used in Paediatric Dentistry - A systematic review', *The Saudi dental journal*, 31(2), pp. 165–172.
 45. Ramesh, A. et al. (2018) 'Comparative estimation of sulfiredoxin levels between chronic periodontitis and healthy patients - A case-control study', *Journal of periodontology*, 89(10), pp. 1241–1248.
 46. Rohini, S. and Kumar, V. J. (2017) 'Incidence of dental caries and pericoronitis associated with impacted mandibular third molar-A radiographic study', *Research Journal of Pharmacy and Technology*, 10(4), pp. 1081–1084.
 47. Roldán-Chicano, R. et al. (2006) 'Panoramic radiograph as a method for detecting calcified atheroma plaques. Review of literature', *Medicina oral, patologia oral y cirugía bucal*, 11(3), pp. E261–6.
 48. Samuel, S. R., Acharya, S. and Rao, J. C. (2020) 'School Interventions-based Prevention of Early-Childhood Caries among 3-5-year-old children from very low socioeconomic status: Two-year randomized trial', *Journal of public health dentistry*, 80(1), pp. 51–60.
 49. Sharma, P. et al. (2019) 'Emerging trends in the novel drug delivery approaches for the treatment of lung cancer', *Chemico-biological interactions*, 309, p. 108720.
 50. Sridharan, G. et al. (2019) 'Evaluation of salivary metabolomics in oral leukoplakia and oral squamous cell carcinoma', *Journal of oral pathology & medicine: official publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology*, 48(4), pp. 299–306.
 51. Steele, J. C. et al. (2015) 'World Workshop on Oral Medicine VI: an international validation study of clinical competencies for advanced training in oral medicine', *Oral surgery, oral medicine, oral pathology and oral radiology*, 120(2), pp. 143–51.e7.
 52. Subashri, A. and Maheshwari, T. N. (2016) 'Knowledge and attitude of oral hygiene practice among dental students', *Research Journal of Pharmacy and Technology*, 9(11), pp. 1840–1842.
 53. Subha, M. and Arvind, M. (2019) 'Role of magnetic resonance imaging in evaluation of trigeminal neuralgia with its anatomical correlation', *Biomedical and Pharmacology Journal*, 12(1), pp. 289–296.
 54. Tofangchiha, M. et al. (2011) 'The carotid artery calcification in type II diabetic patients on panoramic radiographs: An important marker for vascular risk', *Scientific Research and Essays*, 6(31), pp. 6548–6553.
 55. Varghese, S. S., Ramesh, A. and Veeraiyan, D. N. (2019) 'Blended Module-Based Teaching in Biostatistics and Research Methodology: A Retrospective Study with Postgraduate Dental Students', *Journal of dental education*, 83(4), pp. 445–450.
 56. Venugopal, A. and Uma Maheswari, T. N. (2016) 'Expression of matrix metalloproteinase-9 in oral potentially malignant disorders: A systematic review', *Journal of oral and maxillofacial pathology: JOMFP*, 20(3), pp. 474–479.
 57. Vijayashree Priyadharsini, J. (2019) 'In silico validation of the non-antibiotic drugs acetaminophen and ibuprofen as antibacterial agents against red complex pathogens', *Journal of periodontology*, 90(12), pp. 1441–1448.
 58. Vishnu Prasad, S. et al. (2018) 'Report on oral health status and treatment needs of 5-15 years old children with sensory deficits in Chennai, India', *Special care in dentistry: official publication of the American Association of Hospital Dentists, the Academy of Dentistry for the Handicapped, and the American Society for Geriatric Dentistry*, 38(1), pp. 58–59.
 59. Wahab, P. U. A. et al. (2018) 'Scalpel Versus Diathermy in Wound Healing After Mucosal Incisions: A Split-Mouth Study', *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons*, 76(6), pp. 1160–1164.

60. Yoon, S.-J. et al. (2008) 'Diagnostic accuracy of panoramic radiography in the detection of calcified carotid artery', *Dento maxillo facial radiology*, 37(2), pp. 104–108.
61. Zhdanov, V. S. and Sternby, N. H. (2004) 'Monitoring of atherosclerosis', *International journal of cardiology*, 95(1), pp. 39–42.