

# International Journal of Dentistry and Oral Science (IJDOS) ISSN: 2377-8075

# Comparing The Effectiveness Of Various Irrigant Activation Techniques With Conventional Needle Irrigation - A Systematic Review

Research Article

Nivedhitha1\*, Swarna2

<sup>1</sup>Professor and Head, Department of Conservative Dentistry and Endodontics, Saveetha Dental college and Hospital, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India.

<sup>2</sup>Department of Conservative Dentistry and Endodontics, Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India.

#### Abstract

Chemo-mechanical preparation plays a vital role in achieving clinical success in endodontic treatment. Due to varied root morphology, cleaning and shaping cannot be attained by mechanical debridement alone. In vitro studies have confirmed that the irrigant does not penetrate more than 1-2mm beyond the needle orifice. Hence activation of irrigant through various irrigant activation techniques have been tried to improve the efficacy of irrigant penetration into the root canal system. The aim of this study was to comparatively evaluate the microbial reduction in the root canal after Ultrasonic irrigation, Sonic irrigation and Conventional needle irrigation. A search was performed in electronic databases such as PubMed central, Google database and hand search using specific search terms. Only clinical trials were included and the reduction in microbial count were evaluated after ultrasonic and sonic irrigant activation techniques. Five studies fulfilled the study criteria, out of which three studies had high risk of bias and two studies had low risk of bias. To conclude, most of the studies lacked common methodology and more ardent clinical trials are necessary to determine the effectiveness of ultrasonic and sonic irrigation techniques in the microbial reduction of the root canal system.

**Clinical Significance:** The enhancement of irrigant penetration and antimicrobial efficacy of irrigant clinically translates to effective smear layer removal and appropriate disinfection of the root canal system.

Keywords: Conventional Needle Irrigation; Irrigant Activation; Microbial Reduction; Root Canal System; Sonic Irrigation; Ultrasonic Irrigation.

# Introduction

The root canal system has various anatomic diversities and effective cleaning and shaping is complicated by the presence of apical delta, lateral canals, C- shaped canals, fins and isthmuses [1, 2]. Mechanical instrumentation would not reach the anatomical complexities of the root canal system [3]. The microbes in root canal biofilms have a complex structure that is resistant to conventional irrigation [4]. The irrigant penetration is a critical factor in disinfection incases of closed systems such as root canals. Several studies have proved that the irrigant does not penetrate more

than 1-2mm beyond the needle orifice [5, 6]. Various factors such as needle gauge size and length of the needle, open or closed end vented needles, the concentration, temperature and quantity of irrigant used and the intracanal medicament incases of persistent infections are critical factors in achieving successful endodontic outcomes [7, 8]. Sodium hypochlorite has been effectively used for disinfection of root canals but the apical vapor lock needs to be eliminated by irrigant activation techniques [9]. The pressure during irrigation should be controlled in order to avoid extrusion beyond the root apex [10, 11].

Nivedhitha,

Professor and Head, Department of Conservative Dentistry and Endodontics, Saveetha Dental college and Hospital, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India. Email Id: nivedhitha.sdc@saveetha.com

Received: April 28, 2021 Accepted: May 28, 2021 Published: May 30, 2021

Citation: Nivedhitha, Swarna. Comparing The Effectiveness Of Various Irrigant Activation Techniques With Conventional Needle Irrigation - A Systematic Review. Int J Dentistry Oral Sci. 2021;08(05):2626-2631. doi: http://dx.doi.org/10.19070/2377-8075-21000514

Copyright: Nivedhitha<sup>©</sup>2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

Nivedhitha, Swarna. Comparing The Effectiveness Of Various Irrigant Activation Techniques With Conventional Needle Irrigation - A Systematic Review. Int J Dentistry Oral Sci. 2021;08(05):2626-2631.

<sup>\*</sup>Corresponding Author:

Activation of irrigant by sonic, ultrasonic systems and manual dynamic agitation involves mechanical excitation of the irrigant to improve its penetration into the root canal intricacies [12]. The sonic and ultrasonic irrigation involves the processes of cavitation and acoustic streaming which creates oscillations in the irrigant [13]. The manual dynamic agitation is a simple procedure and has been studied for eliminating the vapor lock effect [14, 15]. Various in vitro studies have been done to study the effect of conventional and activated irrigation in smear layer removal, disruption of biofilms, irrigant extrusion, sealer penetration, removal of intracanal medicament and antimicrobial efficacy [16]. Out of all studies, antimicrobial efficacy helps in clinically correlating with disinfection of the root canal system [17]. Previously our team has a rich experience in working on various research projects across multiple disciplines [18-32] Now the growing trend in this area motivated us to pursue this project.

The aim of this systematic review was to determine the effectiveness of various irrigant activation techniques with conventional needle irrigation in microbial reduction of the root canal system.

# Materials and Methods

A literature search was done in PubMed, Cochrane databases and hand search also done. The studies included were clinical trials, prospective and cohort studies comparing the effectiveness of irrigant activation techniques with conventional needle irrigation, in microbial reduction in the root canal system. All case reports, case series, in vitro studies and studies comparing other irrigation activation techniques other than ultrasonic and sonic irrigation techniques with conventional needle irrigation, were excluded from the study. The systematic search is depicted in Figure 1.

# **Results and Discussion**

Our institution is passionate about high quality evidence based

research and has excelled in various fields [22, 33-42]. This leads us towards doing more clinically translatable studies to achieve excellent treatment outcomes.

The search identified 12 publications out of which 2 duplicates were removed. Out of 10 articles, 4 studies were excluded after reviewing the title or abstract and 1 was excluded after reading the full article (Table 1). A total of 5 publications that fulfilled all criteria were included in this review (Table 2, Figure 1).

## **Risk Of Bias Of Included Studies**

The assessment for the four main methodological quality items is shown in the table. The study was assessed to have a 'high risk' of bias if it did not record a 'Yes' in three or more of the main four categories, 'Moderate' if two out of four categories did not record a 'Yes' and 'Low' if randomization assessor blinding and completeness to follow-up were considered adequate (Tables 3 and 4).

The quality assessment of included trials was done after the data extraction process. The method of randomization, allocation concealment, blinding and completeness of follow up were criteria that was examined. The other methodological criteria such as sample size calculation, stringent inclusion and exclusion criteria were also assessed (Figures 2 and 3).

The purpose of this review was to comparatively evaluate the antimicrobial efficacy of sonic, ultrasonic and conventional needle irrigation techniques. Five in vivo studies fulfilled the criteria and were included in the review. Mostly systematic reviews will require meta-analysis, which involves the statistical pooling of data from individual studies when the studies are similar. A meta-analysis can be more predictable for clinical acceptance. However, metaanalysis may not be appropriate in our systematic review, owing to the heterogeneity among the studies such as difference in sample sizes and follow-up periods. Hence, only descriptive evaluation of

S.NO	AUTHOR	YEAR	<b>REASON FOR EXCLUSION</b>
1	Castelo Baz et al.	2012	In vitro Study
2	Eneide et al.	2019	In vitro Study
3	Caputa et al.	2019	In vitro Study
4	Cohenca et al.	2013	Invivo study using dog's teeth

Table 1. Characteristics of Excluded studies.

#### Figure 1. PRISMA Flowchart.



No	Author, year	Study type & design	Outcome variables	Time of Assessment	Statistical test	Intervention	Overall inter- pretation
1	Huffaker et al, 2010	Clinical Sample size – 84 n=42	Colony form- ing units	S1- before cleaning and shaping S2- after cleaning and shaping (1stvisit) S3- after intracanal medicament (2nd visit)	Independent and paired t- test	Group1- Endo Activator Group 2- Standard Irriga- tion	No significant difference between sonic and conventional methods
2	Beus et al, 2012	Clinical N=50 n=25 (PUI) n=25 (CNI)	Colony form- ing units	S1- before instrumentation S2- after irrigation protocol S3- after Ca(OH)2 medicament S4-before obturation		Group 1- Pas- sive ultrasonic irrigation Group 2- Non ultrasonic ir- rigation	No significant difference be- tween irrigation methods
3	Paiva et al, 2013	Clinical Sample Size – n=10	PCR	S1-before root canal instrumentation S2-after root canal instrumentation S3- after irrigation activation	Mean	(NA)	PUI can be inef- fective in signifi- cantly improving disinfection of root canal after chemomechani- cal procedures
4	Her- rera et al, 2016	Clinical Sample size n=24	Microbio- logical assess- ment- CFU counts Endotoxin concentration- LAL assay	S1- before CMP S2- after CMP S3- after EDTA	Friedman's and Wilcoxon signed rank tests	No Groups	Ultrasonic activa- tion of EDTA was efficient in reducing endo- toxin levels in non vital teeth
5	Naka- mura et al, 2017	Clinical N=50 n=25(PUI) n=25(CNI)	Reduction of bacteria- q- PCR Reduction of endotoxin- LAL Assay	S1-before root canal preparation S2-after root canal preparation S3- after irrigation protocol	Kolmogorov- Smirnov test; Wilcoxon test; Mann Whitney test; Chi square test		Ultrasonic activation more effective than non- activated irrigation for reducing bacteria but not the endotoxins in the root canals

Table 2. General information of variables of included studies.

Table 3. Depicts Risk of Bias (Major Criteria).

S.No	Author	Randomi zation	Allocation concealment	Assessor Blinding	Dropouts described	Risk of Bias
1	Huffaker et al.	Yes	Yes	Yes	Yes	Low
2	Beus et al.	No	Yes	No	No	High
3	Paiva et al.	No	No	No	No	High
4	Herrera et al.	No	No	No	No	High
5	Nakamura et al.	Yes	Yes	Yes	None	Low

#### data has been done.

Huffaker et al, evaluated the efficiency of Endo Activator, a sonic irrigation device and conventional needle irrigation, in eliminating microbes in the root canal system. The bacteriological sampling was done before and after cleaning and shaping. An additional microbial sample was taken in the second visit after placement of intracanal medicament. They reported that there was no significant difference between sonic and conventional methods in microbial reduction. But the intracanal medicament seemed to significantly reduce the microbial count during the second visit. This study supported a multi visit approach in treating apical periodontitis [34]. Beus et al, compared the antibacterial efficacy of non-activated single-irrigation protocol (NAI) that used only 1% NaOCl with a Passive ultrasonic multi-irrigation protocol (PUI) that used 1% NaOCl, 17% EDTA and 2% chlorhexidine. The samples were collected before instrumentation, after irrigation protocol, after calcium hydroxide medicament and before obturation. The effect of second visit instrumentation and intracanal medication were also assessed. NAI and PUI made canals 80% and 84% bacteria free, respectively, at the end of the first visit. After medication with calcium hydroxide, it made canals 87% bacteria free, and the second-visit instrumentation made the canals 91% bacteria free. But there was no significant difference between the groups [35].

Paiva et al, evaluated the effects of passive ultrasonic irrigation

S.No	Author	Sample Justified	Baseline Comparison	I/E Criteria	Method Error
1	Huffaker et al, 2010	No	Yes	Yes	No
2	Beus et al, 2012	No	Yes	Yes	No
3	Paiva et al, 2013	No	No	Yes	Yes
4	Herrera et al, 2016	No	Yes	Yes	No
5	Nakamura et al, 2017	Yes	Yes	Yes	No

Table 4. Depicts Risk of Bias (Minor Criteria).

Figure 2. Depicts the risk bias summary [Quality assessment results using risk bias assessment tool outlined in the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0)].



Figure 3. Depicts overall assessment of risk bias [Quality assessment results using risk bias assessment tool outlined in the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0)].



as a supplementary disinfecting step along with a final rinse of 2% chlorhexidine. Samples were taken before and after root canal preparation with 2.5% sodium hypochlorite (NaOCl) irrigation, after either passive ultrasonic irrigation (PUI) for activation of NaOCl or a final rinse with 2% chlorhexidine. The sampling was done using broad-range polymerase chain reaction (PCR) for bacteria, fungi and archaea. There was no significant difference in reduction of microbial load in intergroup comparison [36].

Herrera et al, conducted a clinical study to investigate the effect of Ultrasonic activation of EDTA in reducing endotoxin levels after mechanical debridement of root canals. The samples were taken before and after chemomechanical preparation with M two rotary files, after EDTA irrigation and after ultrasonic activation of irrigant. He concluded that chemomechanical preparation was effective in reducing bacteria and endotoxins, but could not eliminate them completely. The ultrasonic activation of EDTA was efficient in further reducing endotoxin levels in the root canals of teeth with pulp necrosis and apical periodontitis [37].

Nakamura et al, conducted a randomized clinical trial to compare the effectiveness of ultrasonic activation with non-activated irrigation on the removal of bacteria and endotoxin from root canals. They used R40 or R50 Reciproc instrumentation, used 2.5% NaOCl, 17% EDTA as irrigants and Smooth wire 0.2mm diameter and 0.1 taper (Irrisonic) and Piezoelectric ultrasonic device irrigation. Irrigant activation was done using 30G side vented endodontic needle, 2mm short of working length for 30 seconds. Samples were collected before and after root canal preparation and after irrigation protocol. They concluded that ultrasonic activation was more effective than a non-activated irrigation protocol for reducing the number of bacteria but not the endotoxin levels in root canals of teeth with apical periodontitis [43].

#### Interpretation Of The Result

Out of the 5 studies reviewed, it could be inferred that chemo mechanical preparation augmented with irrigant activation was effective in reducing bacterial load and endotoxins but did not completely eliminate them. Considering the fact that there was no significant difference between sonic and conventional methods and between various irrigation methods, it is made clear that newer techniques are needed to completely eliminate the bacterial counts. Also, Passive ultrasonic irrigation was effective in significantly improving disinfection of root canal after chemomechanical procedures. Ultrasonic activation of EDTA led to acoustic

https://scidoc.org/IJDOS.php

streaming and warming of irrigant that helped in reducing endotoxin levels in cases of apical periodontitis [39-41]. Also, the ultrasonic activation is more effective than non-activated irrigation for reducing bacteria but not the endotoxins in the root canals [38]. The outcomes of the studies reviewed, demonstrates the need for irrigant activation for adequate disinfection of the root canal system. Chemo mechanical preparation supplemented with ultrasonic techniques can bring about better disinfection. Polymerase chain reaction is a better tool to assess microbial reduction compared to culture tests as it recognizes a wide range of microorganisms [42]. Among the included clinical trials, only 2 studies have used PCR for microbiological assessment.

### **Implications For Practice**

Effective irrigant penetration and activation is essential for achieving disinfection of the complex root canal system. Mechanical instrumentation with rotary files will not be able to reach the delicate areas of the root canal system. An irrigant must be antimicrobial, act as a lubricant, facilitate smear layer removal, should have tissue dissolving properties and substantivity for prolonged duration of action. The efficacy of the irrigant as well as its penetration is greatly improved by irrigant activation methods. The irrigant activation also helps in reducing the post operative pain [44]. Ultrasonic activation of irrigant along with intracanal medicament as supplementary step, helps in successfully treating apical periodontitis. Thus the therapeutic planning for each case should include the concentration of the irrigant used, type of irrigant activation, intracanal medication [45, 46].

#### **Implications For Research**

Most of the studies regarding the effectiveness of irrigant activation, lack common methodology. More controlled clinical trials with proper randomization, allocation concealment and blinding are necessary to determine the effectiveness of ultrasonic and sonic irrigation techniques in the microbial reduction of the root canal system. Apart from sonic, ultrasonic activation and manual dynamic irrigation, laser irrigation is gaining importance.

### Acknowledgement and Declaration

We would like to acknowledge my mentors and guide for helping me in data collection and analysis and better understanding of systematic review. We declare that the systematic search was performed and risk assessment of studies done to arrive at clinically relevant solutions.

# Conclusion

Ultrasonic irrigation enhanced the penetration of the irrigant in the intricacies of the root canal system. The microbial reduction of ultrasonic irrigation was superior to conventional needle irrigation. There is lack of evidence on endotoxin reduction level with irrigant activation systems. Only two clinical studies on irrigant activation, had a low risk of bias. More ardent clinical trials with strict protocols should be carried out to determine the most effective regimen for irrigant activation.

## References

- [1]. Basrani B, editor. Endodontic irrigation: Chemical disinfection of the root canal system. Springer; 2015 Jul 17.
- [2]. van der Sluis L, Boutsioukis C, Jiang LM, Macedo R, Verhaagen B, Versluis M. Root canal irrigation. InThe root canal biofilm 2015 (pp. 259-301). Springer, Berlin, Heidelberg.
- [3]. Versiani MA, Basrani B, Sousa-Neto MD, editors. The root canal anatomy in permanent dentition. Springer; 2018 Jul 25.
- [4]. de Paz LE, Sedgley CM, Kishen A, editors. The root canal biofilm. Springer; 2015 Oct 20.
- [5]. Boutsioukis C, Lambrianidis T, Verhaagen B, Versluis M, Kastrinakis E, Wesselink PR, et al. The effect of needle-insertion depth on the irrigant flow in the root canal: evaluation using an unsteady computational fluid dynamics model. J Endod. 2010 Oct;36(10):1664-8. Pubmed PMID: 20850673.
- [6]. Boutsioukis C, van der Sluis LW. Syringe irrigation: blending endodontics and fluid dynamics. InEndodontic Irrigation 2015 (pp. 45-64). Springer, Cham.
- [7]. Jain P, editor. Current therapy in endodontics. John Wiley & Sons; 2016 Oct 17.
- [8]. Ng YL, Mann V, Gulabivala K. Outcome of secondary root canal treatment– Systematic review of the literature. International Endodontic Journal. 2007 May;40(5):405-.
- [9]. Sluis LV, Verhaagen B, Macedo RG, Versluis M. Disinfection of the Root Canal System by Sonic, Ultrasonic, and Laser Activated Irrigation. Disinfection of Root Canal Systems: The Treatment of Apical Periodontitis. 2014 Aug 12:217-38.
- [10]. Konstantinidi E, Psimma Z, Chávez de Paz LE, Boutsioukis C. Apical negative pressure irrigation versus syringe irrigation: a systematic review of cleaning and disinfection of the root canal system. International endodontic journal. 2017 Nov;50(11):1034-54.
- [11]. Boutsioukis C, Psimma Z, van der Sluis LW. Factors affecting irrigant extrusion during root canal irrigation: a systematic review. Int Endod J. 2013 Jul;46(7):599-618. Pubmed PMID: 23289914.
- [12]. Gu LS, Kim JR, Ling J, Choi KK, Pashley DH, Tay FR. Review of contemporary irrigant agitation techniques and devices. J Endod. 2009 Jun;35(6):791-804. Pubmed PMID: 19482174.
- [13]. Yoo YJ, Shin SJ, Baek SH. Review of root canal irrigant delivery techniques and devices. Restorative Dentistry and Endodontics. 2011;36(3):180-7.
- [14]. Generali L, Campolongo E, Consolo U, Bertoldi C, Giardino L, Cavani F. Sodium hypochlorite penetration into dentinal tubules after manual dynamic agitation and ultrasonic activation: a histochemical evaluation. Odontology. 2018 Oct;106(4):454-459. Pubmed PMID: 29594826.
- [15]. Machtou P. Manual dynamic activation (MDA) technique. InEndodontic Irrigation 2015 (pp. 149-155). Springer, Cham.
- [16]. Kishen A, Sum CP, Mathew S, Lim CT. Influence of irrigation regimens on the adherence of Enterococcus faecalis to root canal dentin. J Endod. 2008 Jul;34(7):850-4. Pubmed PMID: 18570994.
- [17]. Weber CD, McClanahan SB, Miller GA, Diener-West M, Johnson JD. The effect of passive ultrasonic activation of 2% chlorhexidine or 5.25% sodium hypochlorite irrigant on residual antimicrobial activity in root canals. J Endod. 2003 Sep;29(9):562-4. Pubmed PMID: 14503827.
- [18]. Govindaraju L, Gurunathan D. Effectiveness of Chewable Tooth Brush in Children-A Prospective Clinical Study. J Clin Diagn Res. 2017 Mar;11(3):ZC31-ZC34. Pubmed PMID: 28511505.
- [19]. Christabel A, Anantanarayanan P, Subash P, Soh CL, Ramanathan M, Muthusekhar MR, et al. Comparison of pterygomaxillary dysjunction with tuberosity separation in isolated Le Fort I osteotomies: a prospective, multi-centre, triple-blind, randomized controlled trial. Int J Oral Maxillofac Surg. 2016 Feb;45(2):180-5. Pubmed PMID: 26338075.
- [20]. Soh CL, Narayanan V. Quality of life assessment in patients with dentofacial deformity undergoing orthognathic surgery--a systematic review. Int J Oral Maxillofac Surg. 2013 Aug;42(8):974-80. Pubmed PMID: 23702370.
- [21]. Mehta M, Deeksha, Tewari D, Gupta G, Awasthi R, Singh H, et al. Oligonucleotide therapy: An emerging focus area for drug delivery in chronic inflammatory respiratory diseases. Chem Biol Interact. 2019 Aug 1;308:206-215. Pubmed PMID: 31136735.
- [22]. Ezhilarasan D, Apoorva VS, Ashok Vardhan N. Syzygium cumini extract induced reactive oxygen species-mediated apoptosis in human oral squamous carcinoma cells. J Oral Pathol Med. 2019 Feb;48(2):115-121. Pubmed PMID: 30451321.
- [23]. Campeau PM, Kasperaviciute D, Lu JT, Burrage LC, Kim C, Hori M, et al. The genetic basis of DOORS syndrome: an exome-sequencing study. Lancet Neurol. 2014 Jan;13(1):44-58. Pubmed PMID: 24291220.
- [24]. Sneha S. Knowledge and awareness regarding antibiotic prophylaxis for infective endocarditis among undergraduate dental students. Asian Journal of Pharmaceutical and Clinical Research. 2016 Oct 1:154-9.
- [25]. Christabel SL, Gurunathan D. Prevalence of type of frenal attachment and morphology of frenum in children, Chennai, Tamil Nadu. World J Dent.

2015 Oct;6(4):203-7.

- [26]. Kumar S, Rahman RE. Knowledge, awareness, and practices regarding biomedical waste management among undergraduate dental students. Asian Journal of Pharmaceutical and Clinical Research. 2017;10(8):341.
- [27]. Sridharan G, Ramani P, Patankar S. Serum metabolomics in oral leukoplakia and oral squamous cell carcinoma. J Cancer Res Ther. 2017 Jul-Sep;13(3):556-561. Pubmed PMID: 28862226.
- [28]. Ramesh A, Varghese SS, Doraiswamy JN, Malaiappan S. Herbs as an antioxidant arsenal for periodontal diseases. J Intercult Ethnopharmacol. 2016 Jan 27;5(1):92-6. Pubmed PMID: 27069730.
- [29]. Thamaraiselvan M, Elavarasu S, Thangakumaran S, Gadagi JS, Arthie T. Comparative clinical evaluation of coronally advanced flap with or without platelet rich fibrin membrane in the treatment of isolated gingival recession. J Indian Soc Periodontol. 2015 Jan-Feb;19(1):66-71. Pubmed PMID: 25810596.
- [30]. Thangaraj SV, Shyamsundar V, Krishnamurthy A, Ramani P, Ganesan K, Muthuswami M, et al. Molecular Portrait of Oral Tongue Squamous Cell Carcinoma Shown by Integrative Meta-Analysis of Expression Profiles with Validations. PLoS One. 2016 Jun 9;11(6):e0156582. Pubmed PMID: 27280700.
- [31]. Ponnulakshmi R, Shyamaladevi B, Vijayalakshmi P, Selvaraj J. In silico and in vivo analysis to identify the antidiabetic activity of beta sitosterol in adipose tissue of high fat diet and sucrose induced type-2 diabetic experimental rats. Toxicol Mech Methods. 2019 May;29(4):276-290. Pubmed PMID: 30461321.
- [32]. Ramakrishnan M, Bhurki M. Fluoride, Fluoridated Toothpaste Efficacy And Its Safety In Children-Review. International Journal of Pharmaceutical Research. 2018 Oct 1;10(04):109-14.
- [33]. Vijayashree Priyadharsini J. In silico validation of the non-antibiotic drugs acetaminophen and ibuprofen as antibacterial agents against red complex pathogens. J Periodontol. 2019 Dec;90(12):1441-1448. Pubmed PMID: 31257588.
- [34]. J PC, Marimuthu T, C K, Devadoss P, Kumar SM. Prevalence and measurement of anterior loop of the mandibular canal using CBCT: A cross sectional study. Clin Implant Dent Relat Res. 2018 Aug;20(4):531-534. Pubmed PMID: 29624863.
- [35]. Ramesh A, Varghese S, Jayakumar ND, Malaiappan S. Comparative estimation of sulfiredoxin levels between chronic periodontitis and healthy patients - A case-control study. J Periodontol. 2018 Oct;89(10):1241-1248. Pubmed PMID: 30044495.
- [36]. Ramadurai N, Gurunathan D, Samuel AV, Subramanian E, Rodrigues SJL. Effectiveness of 2% Articaine as an anesthetic agent in children: randomized controlled trial. Clin Oral Investig. 2019 Sep;23(9):3543-3550. Pubmed PMID: 30552590.

- [37]. Sridharan G, Ramani P, Patankar S, Vijayaraghavan R. Evaluation of salivary metabolomics in oral leukoplakia and oral squamous cell carcinoma. J Oral Pathol Med. 2019 Apr;48(4):299-306. Pubmed PMID: 30714209.
- [38]. Mathew MG, Samuel SR, Soni AJ, Roopa KB. Evaluation of adhesion of Streptococcus mutans, plaque accumulation on zirconia and stainless steel crowns, and surrounding gingival inflammation in primary molars: randomized controlled trial. Clin Oral Investig. 2020 Sep;24(9):3275-3280. Pubmed PMID: 31955271.
- [39]. Samuel SR. Can 5-year-olds sensibly self-report the impact of developmental enamel defects on their quality of life? Int J Paediatr Dent. 2021 Mar;31(2):285-286. Pubmed PMID: 32416620.
- [40]. R H, Ramani P, Ramanathan A, R JM, S G, Ramasubramanian A, et al. CYP2 C9 polymorphism among patients with oral squamous cell carcinoma and its role in altering the metabolism of benzo[a]pyrene. Oral Surg Oral Med Oral Pathol Oral Radiol. 2020 Sep;130(3):306-312. Pubmed PMID: 32773350.
- [41]. Chandrasekar R, Chandrasekhar S, Sundari KKS, Ravi P. Development and validation of a formula for objective assessment of cervical vertebral bone age. Prog Orthod. 2020 Oct 12;21(1):38. Pubmed PMID: 33043408.
- [42]. Vijayashree Priyadharsini J, Smiline Girija AS, Paramasivam A. In silico analysis of virulence genes in an emerging dental pathogen A. baumannii and related species. Arch Oral Biol. 2018 Oct;94:93-98. Pubmed PMID: 30015217.
- [43]. Nakamura VC, Pinheiro ET, Prado LC, Silveira AC, Carvalho APL, Mayer MPA, et al. Effect of ultrasonic activation on the reduction of bacteria and endotoxins in root canals: a randomized clinical trial. Int Endod J. 2018 Jan;51 Suppl 1:e12-e22. Pubmed PMID: 28439928.
- [44]. Topçuoğlu HS, Topçuoğlu G, Arslan H. The Effect of Apical Positive and Negative Pressure Irrigation Methods on Postoperative Pain in Mandibular Molar Teeth with Symptomatic Irreversible Pulpitis: A Randomized Clinical Trial. J Endod. 2018 Aug;44(8):1210-1215. Pubmed PMID: 29935873.
- [45]. Prada I, Micó-Muñoz P, Giner-Lluesma T, Micó-Martínez P, Muwaquet-Rodríguez S, Albero-Monteagudo A. Update of the therapeutic planning of irrigation and intracanal medication in root canal treatment. A literature review. J Clin Exp Dent. 2019 Feb 1;11(2):e185-e193. Pubmed PMID: 30805124.
- [46]. Kim D, Kim E. Antimicrobial effect of calcium hydroxide as an intracanal medicament in root canal treatment: a literature review - Part II. in vivo studies. Restor Dent Endod. 2015 May;40(2):97-103. Pubmed PMID: 25984470.