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# Applications of Laser in Endodontic Therapies for the Immature Permanent Tooth: A Systematic Review

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### ABSTRACT

**Purpose:** This systematic review aimed to evaluate the potential benefits of laser-assisted endodontic therapies in the management of immature permanent teeth, compared to conventional treatment approaches. The central research question was: What are the beneficial effects of laser use in endodontic procedures for immature permanent teeth compared to standard techniques?

**Methods:** A comprehensive literature search was conducted across Medline via PubMed, Scopus, and Science Direct databases using relevant MeSH terms. Studies published in English and French between January 2013 and December 2024 were screened based on titles, abstracts, and full-text analysis. Inclusion criteria focused on studies evaluating laser applications in endodontic treatment of immature permanent teeth.

**Results:** From an initial pool of 883 articles, only 2 studies met the inclusion criteria. These studies investigated various laser-assisted procedures, particularly in pulpotomy and regenerative endodontics. Outcomes included assessments of microbial load reduction, clinical success, and root development. While laser techniques showed promising biological and clinical effects, no statistically significant differences were found when compared with conventional methods.

**Conclusion:** Laser technology appears to enhance certain aspects of endodontic therapy in immature permanent teeth by facilitating precise tissue ablation, effective hemostasis, microbial control, and stimulation of tissue regeneration. These advantages support the preservation of pulp vitality and continued root maturation. However, due to the limited number of studies and variability in protocols, further high-quality research is required to establish standardized guidelines and confirm long-term benefits.

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### Introduction

Dental caries and traumatic injuries in immature permanent teeth with incomplete apex formation pose significant challenges to preserving pulp vitality and promoting continued root development and apical closure [1]. Maintaining pulp vitality is essential, as functional pulp tissue exhibits inherent reparative potential and acts as a natural defense mechanism against microbial invasion [2]. In contrast, irreversible pulp damage can lead to necrosis and the arrest of root development. Consequently, the primary therapeutic goal is to preserve pulp vitality, thereby supporting self-repair mechanisms and preventing complications such as infection and incomplete root formation [3].

In this regard, laser therapy has emerged as a promising adjunct in the enhancement of dental pulp regeneration [4]. It has been recognized as a key component in tissue engineering, complementing the triad of stem cells, scaffolds, and growth factors. When appropriately applied, laser therapy stimulates critical cellular functions-including cell proliferation, differentiation, ATP (adenosine triphosphate) production, and protein synthesis-which are essential for tissue repair. Notably, dental pulp stem cells (DPSCs) exhibit a positive response to laser therapy, underscoring the potential of photobiomodulation therapy (PBMT) in stem cell-based strategies for pulp regeneration [5,6].

Laser technology presents a conservative and biologically favorable alternative to traditional pulpotomy agents, due to its regenerative or reparative effects and its capability to sterilize the exposure site. Various laser types have been utilized in pulpotomy procedures, including carbon dioxide (CO<sub>2</sub>), neodymium: yttrium-aluminum-garnet (Nd: YAG), erbium: yttrium-aluminum-garnet (Er: AG), erbium-chromium: yttrium-scandium-gadolinium-garnet (Er, Cr: YSGG), and diode lasers. The choice of laser depends on the thermal relaxation time (TRT) of the target soft tissue—

defined as the time required for the tissue to cool to 50% of its peak temperature following a laser pulse. TRT varies based on tissue vascularity and is highly specific [7].

Furthermore, lasers play an important role in root canal disinfection, a critical step in regenerative endodontic procedures such as revascularization. Laser-assisted disinfection enhances the elimination of bacterial biofilms and pathogens from the root canal system, thereby improving the clinical outcomes of regenerative therapies [8].

The aim of this systematic review is to evaluate the current evidence on the effectiveness and clinical outcomes of laser-assisted therapies—specifically pulpotomy and pulp revascularization—in the management of immature permanent teeth, with a focus on their ability to preserve pulp vitality, promote continued root development, and improve treatment success rates compared to conventional techniques.

## Methods

### Protocol and registration

This systematic review was performed following the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (2020), and it was recorded in the International Prospective Register of Systematic Reviews (PROSPERO database) under the protocol CRD42024501406.

### Review question

The current study aimed to respond to the following question: What are the beneficial effects of using laser in endodontic therapies applied to the immature permanent tooth in comparison with other standard techniques? This question was formulated using the PICOS format, including: (1) Population healthy children, with immature permanent teeth exhibiting reversible or irreversible inflammation or necrosis of the pulp, necessitating endodontic

treatments. (2) Intervention: Laser as a therapeutic approach for the Immature Permanent Tooth. (3) Comparators: Traditional endodontic therapies without laser or a placebo treatment. (4) Outcome: The success of treatment is determined by factors such as the healing of periapical lesions, reduction of symptoms, improvement in clinical and radiographic parameters, and progress in radicular development and apical closure. (5) Study design: randomized controlled trials and prospective cohorts.

### Eligibility Criteria

The inclusion criteria for this systematic review encompassed clinical trials conducted on human subjects, specifically children, that assessed the effectiveness, safety, and overall impact of laser treatment compared to other relevant interventions. The studies included were required to have a clear objective or hypothesis, with detailed information provided on the methodology, including the study design, groups studied, materials, and protocols employed. Additionally, studies were only considered if they reported treatment outcome measures and included a follow-up period of 12 months or more.

### Search Strategy

The search strategy for this systematic review involved a detailed and systematic exploration of three major databases—MEDLINE via PubMed, Science Direct, and Scopus—spanning the period from 2013 to 2024. A predefined set of MeSH terms was employed, including “Laser Therapy,” “Child,” “Root Canal Therapies,” “Apexogenesis,” “Apexification,” “Treatment Outcomes,” “Root Canal Irrigants,” “Dental Pulp,” “Disinfection,” and “Humans.” Boolean operators {AND, OR} were utilized to construct precise search strategies for PubMed, which were subsequently adapted for Scopus and Science Direct using equivalent terms and syntax. A comprehensive summary of the keywords used in the search is provided in Table 1.

**Table 1: Search Strategy**

Database	Search strategy	Results
PubMed	(1) “Dental Pulp” [MeSH Terms] AND “laser therapies” [MeSH Terms] AND “tooth apex” [MeSH Terms] (2) “Root Canal Therapy” [MeSH Terms] OR “methods” [MeSH Terms] AND “laser” [MeSH Terms] AND “dental pulp cavities” [MeSH Terms] AND “desinfection” [MeSH Terms] AND “humans” [MeSH Terms] (3) “laser therapies” [MeSH Terms] AND “canal irrigants root” [MeSH Terms] (4) “laser therapies” [MeSH Terms] AND “child” [MeSH Terms] AND “endodontic treatment” [MeSH Terms] (5) “laser therapies” [MeSH Terms] AND “root canal therapies” [MeSH Terms] AND “tooth apex” [MeSH Terms] (6) “laser therapies” [MeSH Terms] AND “treatment outcomes” [MeSH Terms] AND “endodontics” [MeSH Terms] (7) “laser therapies” [MeSH Terms] AND “apexification” [MeSH Terms] (8) “laser therapies” [MeSH Terms] AND “apexogenesis” [MeSH Terms])	92
Science Direct	(1) “Laser therapy” AND “apexification” AND “immature permanent teeth” (2) “laser therapy” AND “canal irrigant root” AND “immature permanent tooth” (3) “laser therapy” AND “pulp revascularization” AND “immature permanent tooth” (4) “laser therapy” AND “pulpotomy” AND “immature permanent teeth” (5) “laser therapy” AND “treatment outcomes” AND “immature permanent teeth”	535
SCOPUS	(1) “laser” AND “therapies” AND “treatment” AND “outcomes” AND “endodontics” (2) “laser” AND “therapy” AND “apexification” AND “immature” AND “permanent” AND “teeth” (3) “laser” AND “therapy” AND “canal” AND “irrigant” AND “root” AND “immature” AND “permanent” AND “teeth” (4) “laser” AND “therapy” AND “pulpotomy” AND “permanent” AND “teeth” (5) “laser” AND “therapy” AND “pulpotomy” AND “permanent” AND “teeth” (6) “Laser” AND “therapy” AND “pulp revascularization” AND “immature” AND “permanent” AND “teeth”	234

Cochrane Central Register of Controlled Trials	#1[Laser therapy] #2[Canal irrigant root] #3[Tooth] #4[Tooth Apex] #5[Dental Pulp] #6[ Dental pulp capping] #7[Pulpectomy] #8[treatment outcomes] #9 # 1 AND #2 AND #3 #10 #1 AND #4 AND #5 #11 #1 AND #6 #12 #1AND #7AND #3 #13 #1 AND #8 AND #5	22
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### Studies Selection

The search results were then transferred into zotero software, which is used for managing bibliographies and citations. The study selection process unfolded in a three-tiered approach. Initially, focus was solely on the titles of the studies, with the explicit aim of eliminating references that were evidently irrelevant.

Subsequently, the scrutiny extended to the abstracts of the retained studies from the first phase. During this stage, any references deemed irrelevant based on their abstracts were excluded, with additional refinement through a manual search.

In the final step, the full text of the articles that persisted after the abstract screening was meticulously reviewed. This comprehensive process was orchestrated by a trio of reviewers within the workgroup.

Each reviewer independently assessed the titles, abstracts, and full text before convening to compare their findings. Instances of disagreement were resolved through consensus achieved via thoughtful discussion. This meticulous methodology was employed to ensure a thorough and unbiased selection of studies.

### Data Extraction

The data collection process involved the utilization of a pilot-tested spreadsheet for data extraction (refer to Appendix 1), with all procedures carried out by the three reviewers. The pertinent information gathered encompassed various elements, including author details, publication year, publication type, journal information, participant numbers, participant age and gender, the quantity of teeth, diagnosis, details of intervention, follow-up duration, and outcomes. Two distinct tables were employed for extracting information regarding the study protocol and post-treatment outcomes.

It is noteworthy that the data extraction occurred concurrently with the quality assessments of the included studies, signifying a comprehensive and integrated approach to evaluating both the content and methodological rigor of the studies under consideration.

### Evaluating the Risk of Bias

The “Modified Jadad Scale” was used for the assessment of the included studies having the design of randomized controlled trials.

## Results

### Study Selection

An initial search identified 883 potentially relevant results, which were reduced to 398 unique articles after removing duplicates. During the first screening phase, 373 articles were excluded based

on title relevance, leaving 25 for further evaluation. A manual search of their bibliographies yielded no additional relevant studies. Abstract screening in the second phase narrowed the selection to 5 articles. In the final phase, full-text reviews led to the exclusion of 3 articles, resulting in 2 studies being deemed eligible for inclusion in the systematic review (Figure 1).

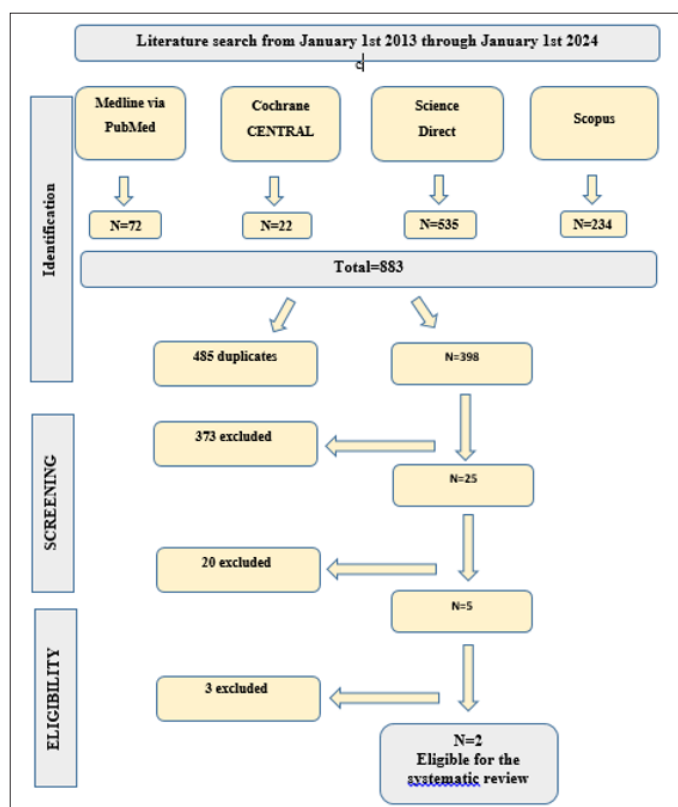


Figure 1: Flow Diagram of the Study Search Process

### Data extraction

#### Characteristics of included studies

The two randomized controlled trials included in this systematic review were published between 2013 and 2023, with the earliest in 2020 and the latest in 2023 [8,9]. Geographically, one study was conducted in Turkey and the other in China. Both trials focused on immature permanent teeth in boys and girls, with participant counts ranging from 66 to 90 and ages spanning 6 to 15 years. Gender information was provided in both studies, and the number of teeth examined matched the participant count. The trials compared two distinct treatment modalities: the first evaluated the efficacy of triple antibiotic paste versus ND: YAP laser for disinfection during pulp regenerative therapy, with outcomes assessed using apical radiographs and cone-beam computed tomography (CBCT) [9].

The second compared the effectiveness of pulpotomy treatment using mineral trioxide aggregate (MTA) alone versus MTA combined with Er, Cr: YSGG laser for immature permanent molars (Table 2) [8].

The studies employed different methodologies, including variations in intervention protocols and outcome assessment techniques, reflecting the diversity of approaches in this field (Table 3).

### Treatment Outcomes

Liu et al compared Triple Antibiotic Paste (control) and Nd: YAP laser (experimental) for pulp regenerative therapy in 66 necrotic teeth, with evaluations conducted at 1 and 2 weeks, then every 3 to 6 months over 24 months. The primary clinical goal-disappearance of symptoms-was achieved in 34 control teeth and 29 experimental teeth at the 24-month follow-up ( $p > 0.05$ ). Radiographic outcomes revealed root wall thickening in 79.2%, continued root development in 76.2%, and positive pulp sensibility in ~60% of cases, though tertiary success rates remained low (~11-13%). CBCT imaging showed high-density pulp calcifications but indicated no adverse effects of laser use, despite limitations such as small sample size and challenges with pediatric imaging (Liu et al 2019). Tozar and Yalmaz compared MTA alone with MTA combined with Er, Cr : YSGG laser for pulpotomy in 90 immature molars, with evaluations at 1, 3, 6, and 12 months. Both groups showed comparable clinical and radiographic outcomes ( $p > 0.05$ ), with success rates of 88.8% for MTA and 95.5% for Laser + MTA. While Laser + MTA demonstrated slightly higher dentin thickening (75.5% vs. 60%), no statistically significant differences were found, and both treatments showed high efficacy with minimal failure rates (Tozar and Yalmaz 2020) (Table 4).

**Table 2: Description of the Included Studies**

Author Year / Journal/ Country	Study title	Number of Participants/ age/teeth	Test/ Control Groups	Aim/ Approach	Follow-up	Laser/ Protocol	Outcome
Tozar et al (2020)/ Journal of Endodontics/ Turkey	Evaluation of the Efficacy of Erbium, Chromium-doped Yttrium, Scandium, Gallium, and Garnet Laser in Partial Pulpotomy in Permanent Immature Molar	90 : 6 to 15 years old/ immature permanent molar teeth	the MTA group (n = 45) and the laser + MTA group (n = 45) the experimental group were disinfected using an Nd:YAP laser (30 patients) the control group were disinfected using a triple antibiotic paste( 36 patients) 20 mL of 2.5% for 5 min, 20 mL of 17% EDTA for 5 min and 50 mL of 0.9% sodium chloride injection without root canal preparation in both groups	Clinical Success: no significant differences between the two groups $p > 0.05$ . Radiographic Success: While the MTA group had slightly fewer cases of radiographic success compared to the laser group this difference was not statistically significant $p = 0.361$ .	1 3 6 And 12 months	The Er, Cr: YSGG laser was used with a noncontact mode. Parameters included 0.5 W energy, 20 Hz repetition rate, and a 140-millisecond pulse duration, with 0% water and 45% air for 10 seconds.	Hard Tissue Formation: 53.3% in the MTA group and 48.8% in the laser group. $p = 0.919$ . Increase in Dentin Thickness: 75.5% compared to the MTA group (60%). $p = 0.117$ . Root Canal Narrowing: A similar proportion of cases in both groups 44.4% in the MTA group and 35.5% in the laser group. $p = 0.727$ .
Liu et al (2023)/ Journal of Clinical Pediatric Dentistry/ china	Effects of an Nd:YAP laser used for root canal disinfection in pulp regenerative therapy	66 aged 8 to 14 years old/ anterior or premolar teeth		Primary goal: Control: 34 teeth symptom-free Experimental: 29 teeth symptom-free Secondary goal: Control: 31 teeth showed radiographic improvement and symptom disappearance in three teeth Experimental: 27 teeth showed similar improvements and symptom disappearance in two teeth Tertiary goal: Four teeth in each group achieved the goal Radiological examination: Both groups showed varying degrees of root canal calcification	3 6 months over a 24-month	Wavelength: 1.34 $\mu$ m Power: 3 W Optical fiber diameter: 0.32 mm Root canal disinfection submenu: Frequency: 30 Hz Power: 100 mJ	Clinical symptoms persisted in 3 teeth (2 control, 1 experimental) with no significant difference. 58 teeth showed satisfactory root development, indicating successful therapy. However, 5 cases resolved symptoms without continued root development or apical closure. Clinical success rates ranged from 71.4% to 97.9%. Approximately 60% exhibited positive pulp sensitivity post-treatment. Tertiary goal success rates were low (11.1% experimental, 13.3% control) due to limited pulp viability.

**Table 3: Protocols of the Selected Studies**  
This table illustrates the protocols of the included studies

Author	Tozar et al	Liu et al
Year	2020	2023
Anaesthesia	Yes	Yes
Rubber Dam	Yes	Yes
Pulp chamber Access	high-speed rotary instrument	NM*
Pulp extirpation	slow-speed sterile steel round bur	NM*
Determination Of work length	No	Preoperative radiographs 1-2 mm short of the Radiographic apex
Canal irrigation Solution	No	-20 mL of 2.5% NaOCl for 5 min - 20 mL of 17% EDTA for 5 min - 50 mL of 0.9% sodium chloride injection - without root canal preparation
Drying the canal root	No	Sterile paper points
Root canal filling	No	NM*
Technique	- Er,Cr:YSGG Laser - Laser used in non-contact mode (0.5 W, 20 Hz, 140 ms pulse) with 0% water and 45% air for 10 seconds.	-Nd : YAP laser : wavelength : 1.34 µm power : 3 W fiber diameter : 32 mm -The laser was set to the disinfection mode (30 Hz frequency, 100 mJ energy). -A light-guiding fiber was inserted approximately 1 mm from the apex of the root. -The fiber was moved up and down along the canal walls for a duration of 30 seconds.
Number of visits	4	4
Final restoration	MTA*+RC*	CR*

MTA\*: mineral trioxide aggregate CR\*: composite resin NM\*: not mentioned

**Table 4: Clinical and Radiographic Findings and Overall, Success Rates based on Postoperative Examination**

	Follow up	Tozar et Yalmaz (2020)				Liu et al (2023)			
		12 months				24 months			
		MTA (n,%)	Laser (n, %)	Total N,%	P value	Triple antibiotic paste (n, %)	Laser (n, %)	Total (n,%)	P value
Clinical findings	SP*	2 (4.5)	1 (2.3)	3 (3.4)	1.00	2(5.6)	1(3.4)	3(4.6)	0.406
	TP*	2 (4.5)	1 (2.3)	3 (3.4)	1.00	2(5.6)	1(3.4)	3(4.6)	0.406
	TTP*	1 (2.3)	0 (0)	1 (1.2)	1.00	2(5.6)	1(3.4)	3(4.6)	0.406
	M*	1 (2.3)	0 (0)	1 (1.2)	1.	2(5.6)	1(3.4)	3(4.6)	0.406
	F*	1 (2.3)	0 (0)	1 (1.2)	1.00	2(5.6)	1(3.4)	3(4.6)	0.406
	S*	2 (4.5)	0 (0)	2 (2.2)	0.495	2(5.6)	1(3.4)	3(4.6)	0.406

Radiographic findings	WPL*	2 (4.5)	1 (2.3)	3 (3.4)	1.00	2(5.6)	1(3.4)	3(4.6)	0.406
	PR*	5 (11.2)	1 (2.3)	6 (6.7)	1.00	2(5.6)	1(3.4)	3(4.6)	0.406
	IR/ER*	1 (2.3)	0 (0)	0 (0)	1.00	2(5.6)	1(3.4)	3(4.6)	0.406
	LLD*	1 (2.3)	0 (0)	0 (0)	1.00	2(5.6)	1(3.4)	3(4.6)	0.406
	CAC*	24 (53.3)	21 (46.6)	45 (50.0)	.596	31(86.1)	27(90.0)	58 (87.9)	0.406
	PAC*	16 (35.6)	22 (48.9)	38 (42.2)	NM*	NM	NM	NM	0.406
	ET*	5 (11.1)	2 (4.5)	7 (7.8)	NM	3(8.4)	2(6.7)	5(7.6)	0.406
	HTF*	24 (53.3)	22 (48.8)	46 (51.1)	.919	NM	NM	NM	0.406
	IDT*	27 (60)	34 (75.5)	61 (67.7)	.117	NM	NM	NM	0.406
	RCN*								
		20 (44.4)	16 (35.5)	36 (40)	.727	31 (86.1)	27 (90.0)	58 (87.9)	0.406
	PRP*	NM	NM	NM	NM	4 (11.1)	4 (13.3)	8 (12.2)	0.406
	OS*	40/45 (88.8)	43/45 (95.5)	83/90 (92.2)	0.435	31/36 (86.2)	27/30 (90.0)	58/90 (87.9)	0.406

SP\*: spontaneous pain TP\*: tenderness to percussion TTP\*: tenderness to palpation M\*: mobility F\*: fistula S\*: swelling WPL\*: widened periodontal ligament PR\*: periapical radiolucency IR/ER\*: internal resorption/external resorption LLD\*: loss of lamina dura CAC\*: complete apical closure PAC\*: partial apical closure ET\*: excluded teeth HTF\*: hard tissue formation IDT\*: increase in dentin thickness RCN\*: root canal narrowing PRP\*: positive results on the pulp sensibility test OS\*:overall success NM\*: not mentioned

### Risk of Bias

The Modified Jadad Scale was utilized to assess the risk of bias in the randomized controlled trials (RCTs) included in this study. This methodological assessment tool consists of an eight-item scale designed to evaluate various aspects such as randomization, blinding, withdrawals and dropouts, adherence to inclusion and exclusion criteria, monitoring of adverse reactions, and the rigor of statistical analysis. Scores on the scale range from 0 (indicating the lowest quality) to 8 (indicating the highest quality). RCTs scoring between 4 and 8 are considered of high quality, reflecting good to excellent methodological rigor, while scores between 0 and 3 indicate poor or low-quality studies.

All included trials demonstrated low risks of methodological bias, characterized by clear delineation of research questions, inclusion and exclusion criteria, and methods of statistical analysis. However, the two trials lacked detailed descriptions of randomization and blinding procedures. Specifically, they provided clear explanations of their randomization methods. Regarding blinding, one trial did not provide any information on blinding methods and the second trial was described as single-blinded (Table 5).

**Table 5: Risk of Bias Evaluation according to the Modified Jaded Scale**

Study	A	B	C	D	E	F	G	H	Total	Score
Tozar et Yalmaz	+1	+1	+1	+1	0	+1	+1	+1	7	High
Liu et al	+1	+1	0	+1	0	+1	+1	+1	6	High

### Discussion

While laser techniques showed promising biological and clinical effects, no statistically significant differences were found when compared with conventional methods.

According to, the use of diode lasers for pulpotomy offers significant advantages due to several key actions [7]. First, diode lasers allow for precise control of hemostasis during the procedure. This means that bleeding can be effectively managed, contributing to improved clinical outcomes.

Additionally, diode lasers create a minimal zone of thermal damage compared to other types of lasers like CO2 or Er: YAG, which helps preserve healthy tissue and promote faster healing. Another critical benefit is the disinfection of the surgical site. Diode lasers have the ability to eliminate or significantly reduce microbial contamination within the pulp stump, providing a more bacteria-free environment conducive to healing.

Moreover, diode lasers are particularly well-suited for use in pediatric patients.

Their non-threatening appearance and reduced tactile sensation compared to other lasers make them more acceptable and comfortable for children undergoing dental procedures. This improved patient experience, coupled with the positive impact on post-operative healing, underscores the effectiveness and suitability of diode lasers in pediatric pulpotomy procedures. The power settings typically used, around 2.0 W, fall within the recommended range as suggested by various sources, ensuring safe and effective treatment outcomes [10,11].

As reported by, the adoption of lasers in pulpotomy procedures represented a notable advancement, with the initial use of CO2 lasers demonstrating significant advantages [12]. These included reduced chairside time and a painless procedure, which enhanced cooperation among pediatric patients.

Among the various types of lasers available, the Diode laser emerged as the most utilized due to its reliability, versatility, and ease of use, complemented by its ergonomic design and straightforward setup. Laser sterilization contributes to comprehensive sterilization protocols, while laser coagulation results in the formation of a thin necrotic layer over the remaining vital pulp, which, in some instances, triggers dentin bridge formation.

In the realm of apexogenesis, addressing pulpal exposure in immature teeth presents clinicians with distinct challenges, particularly in young patients where preserving pulp vitality is crucial for ongoing root development.

Pulpotomy or pulp capping is employed based on the extent of exposure. The utilization of a diode laser (940 nm, Ezlase, Biolase Technology Inc., USA) has proven effective for pulpotomy in traumatized immature permanent teeth. Consequently, the strategic use of soft-tissue diode lasers can significantly impact treatment outcomes, representing a reliable tool for vital pulp therapy [7].

As per analysis, the study findings demonstrate notable differences in success rates among various treatment groups over the follow-up period [13]. The CO<sub>2</sub> laser group consistently achieved the highest success rate, significantly surpassing all other groups. At the twelve-month mark, the CO<sub>2</sub> laser group achieved the highest success rate of 90.1%, while the 980 nm diode laser group achieved a success rate of 80.5% and the Ca (OH)<sub>2</sub> group (79.81%). The Er: YAG laser group (60.58%) and the bioactive tricalcium silicate group (58.6%) had comparatively lower success rates. Importantly, no statistically significant difference was found between the 980 nm diode laser group and the Ca (OH)<sub>2</sub> group, suggesting similar levels of success. However, the Er: YAG and bioactive tricalcium silicate groups showed the least successful outcomes, with no significant difference between them.

By the thirty-six-month follow-up, the CO<sub>2</sub> laser group maintained the highest success rate at 88.01%, followed by the Ca (OH)<sub>2</sub> paste group at 75.72%, the diode laser 980 nm group at 70.01%, the Er laser group at 54.55%, and the bioactive tricalcium silicate group at 51.1%. Importantly, significant differences were found among these groups were observed in success rates among all groups at the thirty-six-month mark.

The null hypothesis was rejected, confirming a difference in success rates between the groups. The study also highlights that laser-assisted Direct Pulp Capping (DPC) yields higher success rates compared to conventional methods, particularly when utilizing the CO<sub>2</sub> laser. The overall ranking of success rates, from highest to lowest, was as follows: CO<sub>2</sub> laser > Ca (OH)<sub>2</sub> > diode laser > Er: YAG laser > bioactive tricalcium silicate [12-15].

In contrast, the study by provides insights into the efficacy of laser-assisted Direct Pulp Capping (DPC) in comparison to traditional methods [8]. Their findings reveal that the use of a laser for biostimulation on the exposed pulpal surface did not significantly improve the success rate compared to MTA alone. Specifically, the success rate for the laser group was 95.5%, which was comparable to the MTA group's success rate of 88.8%. The overall success rate for partial pulpotomy treatment in immature permanent teeth after a twelve-month follow-up was 92.2%. These results suggest that while laser-assisted techniques offer advantages, such as ease of use and minimal risk, they do not necessarily lead to superior outcomes compared to conventional methods like MTA.

Ensuring the success of Regenerative Endodontic Procedures (REPs) hinges on thorough decontamination of the root canal system. This is primarily achieved through a combination of chemical-mechanical preparation techniques. One such method involves the utilization of ultrasonically activated sodium hypochlorite (NaOCl) in conjunction with ethylenediaminetetraacetic acid (EDTA). Additionally, the incorporation of antibiotics can enhance the effectiveness of this process.

The standard protocol for revascularization in endodontic therapy has notable limitations, primarily due to the absence of mechanical canal preparation. This lack of instrumentation leaves residual bacterial biofilm on the canal walls, which can compromise the success of the treatment. Moreover, the use of intracanal antibiotics and calcium hydroxide, common in traditional revascularization, can be associated with undesirable effects such as bacterial resistance, antibiotic allergies, tooth discoloration, and a reduction in the strength of the radicular wall.

In contrast, laser-assisted revascularization offers an alternative approach with potential advantages. The use of lasers in canal disinfection may provide more effective bacterial elimination while avoiding some of the side effects related to antibiotic use. Additionally, lasers can minimize the weakening of the radicular wall, making it a promising alternative to conventional techniques [16].

According to the available literature does not provide conclusive evidence that laser-assisted irrigation significantly improves the clinical success of regenerative endodontic therapy (RET) [17]. However, some studies suggest that laser-assisted disinfection (LAD), using diode or Nd lasers, can achieve bacterial reduction in necrotic root canals comparable to that of triple antibiotic paste. Moreover, LAD appears to offer slightly superior clinical and radiographic outcomes compared to standard techniques without laser irradiation. Photodynamic therapy (PDT) has shown promise as an effective adjunct to traditional canal disinfection methods, particularly in immature permanent teeth with pulp necrosis.

Furthermore, low-power lasers may prove to be valuable tools in enhancing the success of regenerative procedures. In the first phase, they can aid in chemical disinfection through PDT, and in the second phase, they can stimulate tissue healing via photo biomodulation therapy (PBMT), making them a potentially powerful addition to RET protocols [17].

According to, photo biomodulation therapy (PBMT) has been shown to have a range of positive effects on stem cells [6]. These effects encompass the promotion of stem cell growth, augmentation of their metabolic processes, enhancement of regeneration capabilities, particularly notable in dentine regeneration following pulp exposure, and favorable influences on the viability and differentiation of mesenchymal stem cells derived from dentoalveolar tissues. Encouraging outcomes from preclinical studies, including those exploring pulp regeneration via PBMT-based Regenerative

Endodontic Procedures (REPs), suggest the potential of this approach as a feasible alternative to cell-homing therapies [18].

Based on insights gleaned from a systematic review of Eugenia Anagno, cutting-edge conventional endodontic therapy techniques persist as the established "gold standard" treatment [19]. However, the variability in reported failure rates and post-operative discomfort has spurred the exploration of supplementary

options. In this regard, laser utilization has undergone extensive scrutiny. The analysis revealed that nearly all studies demonstrated a statistically significant enhancement in outcomes with laser-assisted endodontic therapy. Consequently, lasers can be recommended as advantageous adjunctive treatment modalities.

Concerning the safety of this treatment, the absence of comprehensive parameter reporting, particularly notable in photo biomodulation therapy (PBMT) and antimicrobial photodynamic therapy (aPDT), complicates the formulation of definitive conclusions. Irradiation protocols should be approached judiciously, especially regarding thermal fluctuations in the root canal system and surrounding tissues. A burgeoning interest in researching pain modulation within this domain is evident. Moving forward, conducting additional studies with clear and standardized protocols will be imperative to further corroborate the evidence base of this approach [20,21].

According to, 0.5% sodium hypochlorite (NaOCl) was utilized as the sole disinfectant, Enhanced by Er: YAG laser irrigation, aiming to achieve revascularization of periapical periodontitis through the use of concentrated growth factors (CGF) [22]. This approach was designed to accomplish apical closure, facilitate root development, and preserve physiological function. Er: YAG irrigation demonstrated notable effectiveness as a root canal disinfection protocol, offering advantages such as ease of operation and minimal risk. These attributes suggest its potential applicability to revascularization of necrotic immature permanent teeth. Nevertheless, further high-quality clinical studies are imperative to establish robust scientific evidence that firmly supports this assertion (Anagnostaki et al.2020; Lintong et al. 2022) [19].

In addition, study presents promising findings regarding Nd laser irradiation as an alternative to triple antibiotic paste for pulp disinfection [9]. This method showed effectiveness in the context of pulp regenerative therapy, though additional research is required to confirm these results and ensure long-term success. The study also highlighted the utility of both apical radiographs and Cone Beam Computed Tomography (CBCT) in evaluating treatment outcomes. CBCT emerged as superior for detailed analyses compared to apical radiographs, despite challenges in acquiring images in pediatric patients. Importantly, no significant negative effects of the Nd laser on the prognosis of pulp regenerative therapy were observed.

### **Limitation**

The present review faced challenges during data extraction, affecting the reliability of the included studies. Both articles share significant limitations, including small sample sizes, short follow-up periods, and a lack of blinding or control measures, which increase susceptibility to bias and reduce the generalizability of findings. Methodological issues, such as inadequate control groups and absence of randomization, further weaken their validity. These weaknesses must be acknowledged when interpreting the studies' implications for clinical practice.

### **Recommendation**

Based on the findings of this systematic review, laser-assisted

therapies show promise as valuable adjuncts in the management of immature permanent teeth, particularly in procedures such as pulpotomy and pulp revascularization. However, their integration into routine clinical practice should be approached with caution until standardized protocols—particularly regarding laser parameters such as wavelength, power output, and duration—are established. Further high-quality randomized controlled trials with adequate sample sizes and long-term follow-up are essential to confirm the efficacy, safety, and predictability of these interventions. Additionally, future research should assess the cost-effectiveness and accessibility of laser technologies in various clinical settings. The development of comprehensive training programs and evidence-based clinical guidelines will also be crucial to support the safe and effective use of lasers in pediatric endodontics.

### **Conclusion**

The use of laser technology in the treatment of immature permanent teeth, particularly in procedures like pulpotomy and pulp revascularization, marks a significant advancement in endodontic practice. Lasers offer unparalleled precision in removing diseased tissue while preserving healthy pulp, fostering an environment for reparative dentinogenesis and improving success rates. In pulp revascularization, lasers enhance disinfection, support stem cell recruitment, and promote angiogenesis, accelerating the restoration of pulp vitality and continued root development.

While the current evidence shows promising results, further research is needed to optimize laser parameters, standardize protocols, and evaluate long-term outcomes. Addressing these gaps will refine clinical practices and improve the predictability and efficacy of laser-assisted treatments for immature permanent teeth. Ultimately, laser-based therapies serve as a valuable adjunct to traditional methods, offering new opportunities for successful outcomes and the preservation of dental function in pediatric patients.

### **Funding**

This review received no grant from any funding agency in the public commercial or not for profit sectors.

### **Data Availability**

All relevant data (Flowchart, tables) are available on request.

### **Conflict of interest**

All authors declare no conflict of interest.

### **Consent to Participate**

Not applicable.

Ethics Approval

Not applicable.

### **Clinical Trial Number**

Not applicable.

### **Human Ethics and Consent to Participate Declarations**

Not applicable.

Eight items	Answer	Score
1. Was the study described as randomized?	Yes	+1
	No	0
2. Was the method of randomization appropriate?	Yes	+1
	No	-1
	Not described	0
3. Was the study described as blinding? <sup>a</sup>	Yes	+1
	No	0
4. Was the method of blinding appropriate?	Yes	+1
	No	-1
	Not described	0
5. Was there a description of withdrawals and dropouts?	Yes	+1
	No	0
6. Was there a clear description of the inclusion/exclusion criteria?	Yes	+1
	No	0
7. Was the method used to assess adverse effects described?	Yes	+1
	No	0
8. Was the method of statistical analysis described?	Yes	+1
	No	0

**Note:** <sup>a</sup>Double-blind got 1 score; single-blind got 0.5 score.

Appendix 1: The modified jadad scale

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	The Impact of Breastfeeding Duration on Dental Caries and Malocclusion in Primary Dentition : A Systematic Review	
ABSTRACT			
Abstract	2	<p>Purpose:This systematic review explores whether the duration of breastfeeding affects the occurrence of dental caries and malocclusion in primary dentition. By addressing gaps and conflicting findings in the literature, it aims to provide clinically relevant evidence that can help guide recommendations on the optimal duration of breastfeeding to support both oral health and early childhood development. The review question was: Does the duration of breastfeeding have an impact on the occurrence of dental caries and malocclusion in primary dentition?</p> <p>Methods:A systematic review was conducted following PRISMA guidelines. Searches were performed in PubMed, Scopus, cochrane library and Web of Science . The literature search was performed using MeSH terms and relevant keywords related to breastfeeding, early childhood caries, and malocclusion. Study selection, data extraction, and quality assessment (using the Newcastle-Ottawa Scale) were carried out independently by three reviewers.</p> <p>Results:A total of 10 cohort and cross-sectional studies from diverse geographic regions met the inclusion criteria. The results showed a trend toward increased risk of dental caries with prolonged breastfeeding beyond 12 months, particularly when nocturnal feeding and lack of oral hygiene were reported. The risk appears to rise progressively up to 18 months and becomes more significant by 24 months. Conversely, longer breastfeeding duration (&gt;12 months) was associated with a reduced prevalence of malocclusions, especially compared to early weaning or prolonged bottle-feeding.</p> <p>Conclusion:Breastfeeding duration appears to have a differential impact on oral health: while extended breastfeeding may slightly increase caries risk under specific conditions, it may protect against the development of malocclusions. Preventive guidelines should consider both feeding duration and oral hygiene practices to optimize early childhood oral health.</p>	
INTRODUCTION			

Rationale	3	<p>Dental caries and malocclusion are among the most prevalent oral conditions in early childhood, with significant implications for oral health, function, and quality of life. Early childhood caries (ECC) is defined as the presence of one or more decayed, missing (due to caries), or filled tooth surfaces in any primary tooth in a child under the age of 71 months (Chen et al.2019). Malocclusion, on the other hand, is a developmental anomaly influenced by both genetic and environmental factors that affects the maxillofacial structures, including the jaws, tongue, and surrounding soft tissues (Meza et al.2017).</p> <p>Many of these developmental disruptions originate during the first year of life when primary dentition and orofacial structures begin to form (de Vasconcelos et al.2021). While breastfeeding is generally regarded as beneficial,(van Meijeren et al .2021) emerging evidence suggests that prolonged breastfeeding beyond 12 to 24 months, especially when combined with poor oral hygiene or nighttime feeding, may be associated with an increased risk of dental caries. (Ham et al.2015 ; Shrestha, et al.2024) This apparent paradox highlights the complexity of the relationship between breastfeeding and oral health, and underscores the importance of evidence-based guidance.</p> <p>Although previous systematic reviews have explored the associations between breastfeeding and either early childhood caries or malocclusion separately, no study to date has synthesized evidence on both conditions simultaneously in the context of primary dentition.</p>	
Objectives	4	this systematic review aims to evaluate the association between breastfeeding duration and the prevalence of dental caries and/or malocclusion in the primary dentition, in order to inform evidence-based prevention strategies in pediatric oral health care.	
METHODS			
Eligibility criteria	5	This systematic review included studies conducted on healthy children with primary dentition that examined the impact of breastfeeding duration on dental caries and malocclusion, provided clear definitions of breastfeeding duration, and reported oral health outcomes specific to primary dentition. Only studies published in English or French were considered. Studies were excluded if they involved children with mixed or permanent dentition, special health needs, lacked precise measures of breastfeeding duration, focused solely on artificial feeding, or addressed outcomes unrelated to caries and malocclusion.	
Information sources	6	A systematic search using key words was conducted using four databases;Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE via PubMed, Science Direct, Scopus. The search covered the period from January 1st 2020 to January 1st 2025 and it was updated throughout the redaction of this systematic review.A selection of “MeSH terms” was used. Then, using the Boolean (AND, OR) commands allowed building research strategies for pubmed. An appropriate search strategy was established for Scopus and Science Direct and cochrane.	
Search strategy	7	<p>Pubmed (1) (“Breast Feeding”[Mesh] AND (“Dental Caries”[Mesh] OR “Tooth demineralization “[Mesh])</p> <p>(2) (“Breast Feeding”[Mesh] AND (“Malocclusion”[Mesh] OR “Open Bite”[Mesh] OR “overbite”[MeSH Terms] OR “Maxillofacial Development”[Mesh])</p> <p>ScienceDirect (1)breastfeeding AND duration AND (“dental caries” OR “early childhood caries”)</p> <p>(2) breastfeeding AND duration AND (“malocclusion” OR “open bite” OR “crossbite” OR “overbite” OR “crowding”)</p> <p>Scopus (1) breastfeeding AND duration AND dental AND caries AND primary AND dentition</p> <p>(2)breastfeeding AND duration AND early AND childhood AND caries AND primary AND dentition</p> <p>(3)breastfeeding AND duration AND malocclusion AND primary AND dentition</p> <p>(4)breastfeeding AND duration AND dental AND crowding AND primary AND dentition</p> <p>Cochrane (1) (“breastfeeding”) AND (“dental caries”) AND (“primary dentition”)</p> <p>(2)(“breastfeeding”) AND (“malocclusion”) AND (“primary dentition”)</p>	
Selection process	8	<p>The electronic search results were then imported into zotero and duplicated records were discarded.</p> <p>The selection of studies was conducted in three stages:Initially, only the titles of the studies were reviewed, and any obviously irrelevant references were excluded. Next, the abstracts of the remaining studies were screened, and studies deemed irrelevant based on their abstracts were excluded.At this stage, hand searching in the references of included papers was performed to eventually retrieve any study that was not identified during the primary search . Finally, the full texts of the remaining articles were reviewed to determine whether they met the inclusion criteria.</p>	

Data collection process	9	The data collection process involved the utilization of a pilot-tested spreadsheet for data extraction , with all procedures carried out by the three reviewers.	
Data items	10a	The pertinent information gathered encompassed various elements, including Author(s),Year of publication,Country of the study Study design ,Sample size,Age of children ,Information on feeding habits, Diagnosis of dental caries and malocclusions, Modifying factors, Main findings	
	10b	Author(s),Year of publication,Country of the study Study design ,Sample size,Age of children ,Information on feeding habits, Diagnosis of dental caries and malocclusions, Modifying factors, Main findings	
Study risk of bias assessment	11	The “New castle ottawa-scale Scale” was used for the assessment of the included studies having the design of cohort and cross- sectional studies.	
Effect measures	12	No effect measure(s) was used	
Synthesis methods	13a	Due to the heterogeneity of the papers, a meta-analysis was not appropriate to review the findings.	
	13b	Due to the heterogeneity of the papers, a meta-analysis was not appropriate to review the findings.	
	13c	Due to the heterogeneity of the papers, a meta-analysis was not appropriate to review the findings.	
	13d	Due to the heterogeneity of the papers, a meta-analysis was not appropriate to review the findings.	
	13e	Due to the heterogeneity of the papers, a meta-analysis was not appropriate to review the findings.	
	13f	Due to the heterogeneity of the papers, a meta-analysis was not appropriate to review the findings.	
Reporting bias assessment	14	Due to the heterogeneity of the papers, a meta-analysis was not appropriate to review the findings.	
Certainty assessment	15	Due to the heterogeneity of the papers, a meta-analysis was not appropriate to review the findings.	
<b>RESULTS</b>			
Study selection	16a	A total of 495 results were recorded. 355 articles were remained after removing 140 duplicated articles. Then the exclusion of 315 references. In this phase, only the title of each research result was screened to eliminate clearly irrelevant references. 40 articles were approved as they were eligible to the second phase. After reading through the abstracts 13 were left to next phase. At this stage, a manual search through more publications was carried out, in order to find all the relevant research and this was through references of selected studies and relevant systematic reviews of the topic meeting the inclusion criteria one article was added after considering the inclusion of criteria. 10 articles were considered eligible for this systematic review	
	16b	Out of topic Mixed /permanent dentition Breastfeeding not a control group outcomes or conditions unrelated to caries and malocclusion. Breastfeeding duration not categorize	
Study characteristics	17	Study description Of the 10 papers selected,four were cross-sectional, six cohort studies .The studies were predominantly conducted in high and middle income countries with only one study from low income countries. The majority (90 % ) of the studies were published from 2020 to 2023. Population/sample The overall study sample was 17332 children with an average age range of 0 –5 years. studies recruited children from maternity hospitals or public health facilities (Sritangsirikul et al.2024; van Meijeren et al .2021 ; Devenish et al.2020; Tesfay et al 2024;Mathias et al.2024 ; Duraisamy et al.2020). by complex random sampling (Chiao et al.2021), randomly from rural and urban region from all over the country(Kalita et al.2023; Sæthre et al.2023), from national child vaccination program list (Barroso et al.2021) .The population included participants from both genders.	
Risk of bias in studies	18	The level of evidence and risk of bias were assessed using the Newcastle-Ottawa Scale (NOS), adapted for both cohort and cross-sectional studies. Among the included studies, 60% of the cohort studies were rated as having a low risk of bias. In contrast, 30% of the cross-sectional studies presented a moderate risk of bias, while 10% showed a high risk of bias.	
Results of individual studies	19	Due to the heterogeneity of the papers, a meta-analysis was not appropriate to review the findings.	

Results of syntheses	20a	Due to the heterogeneity of the papers, a meta-analysis was not appropriate to review the findings.	
	20b	Due to the heterogeneity of the papers, a meta-analysis was not appropriate to review the findings.	
	20c	Due to the heterogeneity of the papers, a meta-analysis was not appropriate to review the findings.	
	20d	Due to the heterogeneity of the papers, a meta-analysis was not appropriate to review the findings.	
Reporting biases	21	Due to the heterogeneity of the papers, a meta-analysis was not appropriate to review the findings.	
Certainty of evidence	22	Due to the heterogeneity of the papers, a meta-analysis was not appropriate to review the findings.	
DISCUSSION			

Discussion	23a	<p>This review highlights a protective association between exclusive breastfeeding during the first months of life and reduced risk of dental caries. However, an increased risk begins to emerge after 12 months, particularly in the context of prolonged nocturnal breastfeeding without proper oral hygiene. The risk appears to rise progressively up to 18 months and becomes more significant by 24 months, coinciding with the eruption of additional primary teeth and greater exposure to cariogenic foods and feeding behaviours.</p> <p>The American Academy of Pediatric Dentistry (AAPD) supports breastfeeding for at least 12 months due to its well-documented benefits for infant health, development, and psychosocial well-being.(AAPD 2023). However, the AAPD advises caution regarding unrestricted nocturnal breastfeeding after the eruption of the first primary tooth, as this practice may elevate the risk of early childhood caries (ECC). These recommendations align with our findings, which suggest a relatively low caries risk during the first year of life, followed by an increased risk beyond 12 months—particularly in the presence of prolonged nocturnal breastfeeding without appropriate oral hygiene practices. These findings are consistent with the systematic review conducted by (Shrestha et al.2024).</p> <p>A “safe window” for breastfeeding in relation to caries risk appears to lie between 6 to 18 months, with the lowest risk observed up to 12 months. This aligns with the eruption pattern of the primary dentition. The maxillary and mandibular incisors, which are among the most susceptible to early childhood caries, typically erupt between 6 and 12 months, while the first primary molars—also at high risk—emerge between 13 and 19 months.(The American Dental Association 2005)</p> <p>Only one study in the review addressed the impact of BF duration on malocclusion, finding A notable reduction in the prevalence of malocclusions is observed when the duration of breastfeeding exceeds 12 months. Prolonged bottle-feeding beyond 12 months appears to be a factor associated with a higher prevalence of malocclusions. However this association is not statistically significant association .(Duraisamy et al. 2020)</p> <p>The orofacial development is thought to be influenced by early feeding modes. Breastfeeding reinforces the physiological nasal breathing of the newborn during and after sucking of breast milk, avoiding oral breathing and thus preventing the development of malocclusions .( Peres et al.2015)</p> <p>The act of breastfeeding is positively associated with the development of dental arches in the temporal dentition in the anterior transverse and sagittal plane.(Sum et al.2015)</p> <p>Breastfeeding promotes coordinated activity of the tongue, lips, and jaw, supporting the proper development of orofacial structures and potentially lowering the risk of malocclusion.(Viggiano et al.2004)</p> <p>This is due to the active “squeeze action” required to extract milk from the breast, which engages the oral musculature more fully. In contrast, bottle-feeding often involves a more passive sucking mechanism that provides less stimulation to these structures and may contribute to the development of dysfunctional oral habits over time.(Silveira et al.2013)</p> <p>According to (Chen, X et al.2015) Children who were fed by the bottle for a period of time greater than 18 months have a risk greater than 1.6%, 1.16% and 1.43% of having, respectively, posterior cross bite, maxillary compression and canine Class II than children who received said feeding until 18 months.</p> <p>The results of (Gomes et al.2006) suggest that there is similarity in the muscular activity of masseter, temporalis and buccinators in children fed exclusive breastfeeding and even supplemented with cup feeding; Therefore, the latter can be used as an alternative infant feeding method, improving its action on the bottle, due to the hyperactivity of the buccal muscles that could lead to changes in the structural growth and development of the stomatognathic system</p> <p>Many studies suggest that a BF for short period is related to an increased risk of malocclusion (Boronat-Catalá et al.2019; Thomaz et al. 2012). This is in accordance with our findings that suggests that a BF for less than 6months is related to an increased risk of malocclusion</p>	
	23b	<p>The review revealed considerable heterogeneity in caries diagnosis criteria. This lack of standardization in defining and reporting ECC complicates both inter-study comparison and meta-analytic synthesis. Additionally, a reliance on cross-sectional designs in several studies limits causal inference, as temporal sequences between BF exposure and caries and/or malocclusion development cannot be firmly established . Cohort studies provided stronger evidence, though many still faced limitations such as self-reported feeding data, recall bias, and inconsistent adjustment for dietary and socioeconomic confounders</p>	
	23c	<p>The scarcity of longitudinal studies linking feeding behaviors to malocclusion outcomes represents a critical research gap. Orthodontic research should integrate early life feeding histories into assessments of occlusion, particularly given the preventable nature of some early malocclusions.</p>	

	23d	Based on the findings of this systematic review, laser-assisted therapies show promise as valuable adjuncts in the management of immature permanent teeth, particularly in procedures such as pulpotomy and pulp revascularization. However, their integration into routine clinical practice should be approached with caution until standardized protocols—particularly regarding laser parameters such as wavelength, power output, and duration—are established. Further high-quality randomized controlled trials with adequate sample sizes and long-term follow-up are essential to confirm the efficacy, safety, and predictability of these interventions. Additionally, future research should assess the cost-effectiveness and accessibility of laser technologies in various clinical settings. The development of comprehensive training programs and evidence-based clinical guidelines will also be crucial to support the safe and effective use of lasers in pediatric endodontics.	
OTHER INFORMATION			
Registration and protocol	24a	CRD42025635783	
	24b	The International Prospective Register of Systematic Reviews (PROSPERO database)	
	24c	no amendments to information have been made.	
Support	25	This review received no grant from any funding agency in the public commercial or not for profit sectors.	
Competing interests	26	All authors declare no conflict of interest	
Availability of data, code and other materials	27	The new castle ottawa scale available (appendix).	

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