



## REVIEW ARTICLE



## Management of Immature Permanent Necrotic Teeth Treated by Regenerative Endodontic: A Systematic Review

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## ARTICLE INFO

## ABSTRACT

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**Keywords:**  
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**Background:** Regenerative endodontics is an evolving field of dentistry that focuses on biological restoration and tissue regeneration rather than traditional apexification techniques. This approach utilizes biological materials, growth factors, and scaffolds to stimulate natural healing, enabling root dentin thickening and lengthening. Regenerative endodontic procedures (REPs) aim to replace damaged structures, relieve symptoms, promote bone healing, and enhance root maturation. The success of REPs relies on three key components: stem cells, signaling molecules, and an appropriate scaffold to support cell growth and differentiation.

**Methods:** This systematic review evaluates the management of immature permanent necrotic teeth treated with regenerative endodontic procedures. A comprehensive literature search was conducted in PubMed and Google Scholar databases for studies published between 2015 and 2024, following PRISMA guidelines. Case series and case reports were included based on predefined eligibility criteria. Data extraction focused on patient demographics, etiology, radiographic findings, treatment protocols, and clinical outcomes.

**Results:** The findings indicate that regenerative endodontic treatment is highly effective, with a success rate of 82.6%, demonstrating significant healing of pre-apical radiolucency and root maturation. The most commonly used irrigation protocol involved NaOCl, saline, and EDTA, while Triple Antibiotic Paste (TAP) was the preferred intracanal medicament. MTA was the most frequently used capping material, and Platelet-Rich Fibrin (PRF) and Blood Clot (BC) were the most commonly utilized scaffolds. Despite the high success rate, a small percentage of cases were only partially successful or failed, emphasizing the need for further research to refine treatment protocols and improve long-term outcomes.

**Conclusion:** This review highlights the importance of regenerative endodontic techniques in promoting root development and peripapical healing, offering a biologically driven approach to managing immature necrotic teeth. Further studies are required to optimize treatment strategies and enhance clinical predictability.



### Introduction

Regenerative endodontics is a novel and evolving branch of regenerative dentistry that focuses

on biological restoration and natural tissue regeneration rather than traditional methods like

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apexification. This approach utilizes biological materials and growth factors to stimulate the natural healing process, enabling root dentin thickening and lengthening through the regeneration of vital tissue (1, 2). A regenerative endodontic procedure (REP) is a biologically based treatment designed to replace damaged structures, including dentin, root structures, and the pulp-dentin complex. The concept of revascularization, which serves as the foundation for regenerative endodontics, was first introduced by Ostby in 1960, and since then, it has evolved into an innovative treatment protocol in endodontics (3, 4). The main objectives of regenerative endodontic procedures (REPs) are to relieve symptoms, facilitate bone healing, and enhance root wall thickness, root length, and overall vitality. REPs have been highly effective in treating necrotic immature teeth, consistently achieving high success and survival rates (5). The periapical tissues of immature teeth are rich in blood vessels and contain stem cells capable of self-renewal and repairing damaged areas when properly stimulated (6). The success of a regenerative endodontic procedure relies on three key components: stem cells, which contribute to the formation of new hard tissue; signalling molecules, which stimulate and guide cellular differentiation; and a three-dimensional scaffold, which provides structural support for cell growth and development (7). An appropriate scaffold is a crucial element in regenerative endodontic strategies (8). It should be porous, biodegradable, biocompatible with the surrounding tissues, and possess the correct shape to facilitate the replacement of lost tissues (1). While not a true scaffold, many clinicians use blood clots (BLCs) in the root canal to serve this purpose. Alternatives like platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) offer higher platelet concentrations and essential growth factors (e.g., PDGF, TGF, IGFs, VEGF, EGF, ECGF) compared to blood clots, which primarily consist of red blood cells. These autologous platelet concentrates enhance regeneration, though outcomes may vary (8). PRF as an autologous biomaterial composed of leukocytes, platelets, and healing proteins within a dense fibrin matrix. It acts as a reservoir for bioactive molecules, releasing them gradually over 7–14 days, promoting cell proliferation, differentiation, and angiogenesis. Additionally, its leukocytes, cytokines, and lymphocytes contribute to inflammation regulation

and infection control, supporting tissue healing (9). Triple antibiotic paste (TAP), consisting of metronidazole, ciprofloxacin, and minocycline, is the most commonly used intra-canal medicament in endodontic regeneration. However, to prevent the discoloration associated with minocycline in TAP, double antibiotic paste (DAP), which includes only metronidazole and ciprofloxacin, has been recommended and effectively used in endodontic regeneration (10). After applying a scaffold within the canal, it is essential to create a coronal bacteria-tight seal. MTA is commonly chosen as a material for this seal in regenerative procedures. Currently, various bioceramic cements, such as bioaggregate and biodentine (a bioactive dentine substitute, is a tricalcium silicate-based material), are available for use in endodontics. These materials are preferred over gray MTA because they do not cause discoloration (11).

The aim of this systematic review is to collect and analyze existing evidence on the management of immature permanent necrotic teeth treated with regenerative endodontic procedures. By reviewing relevant studies and credible data, this study evaluates the success rates, advantages, and limitations of various pulp regeneration approaches, including the use of intracanal medicaments, bioceramic materials, and tissue engineering techniques. Additionally, this research seeks to identify and recommend the most effective treatment strategies based on scientific evidence to improve the prognosis of these teeth.

## Methodology

### Search Strategy

An electronic search was conducted to identify relevant studies published in English between 2015 and 2024 using PubMed and Google Scholar databases. The search was performed following the PRISMA guidelines, utilizing Boolean operators ("AND" and "OR") to refine the search results. The keywords used included: 'immature teeth' OR 'immature dentition' AND 'pulp revascularization' OR 'pulpal regeneration' OR 'regenerative endodontic' AND 'blood clot' OR 'platelet-rich fibrin' AND 'apical closure' OR 'root end formation'. A detailed description of the search strategy and the number of results retrieved is presented in Table 1.

### **Inclusion and Exclusion Criteria**

The selection of studies was based on the following inclusion criteria:

- In vivo studies conducted in humans in which Regenerative Endodontic Treatment (RET) was performed.
- Studies published in English.
- Studies published between 2015 and 2024.
- Evaluation of treatment outcomes based on clinical and radiographic examinations.
- The success rate was reported or calculable from the provided data.
- Study types included case series and case reports.

Studies were excluded if they met any of the following criteria:

- In vitro studies.
- Studies that did not involve RET (e.g., conventional endodontic treatment, apexification).
- Studies published in languages other than English.
- Studies published before 2015 or after 2024.
- Studies that did not assess treatment outcomes using clinical and radiographic evaluations.
- Studies with study designs other than case series and case reports (e.g., randomized controlled trials, cohort studies, systematic reviews, or narrative reviews).

### **Study Selection and Data Extraction**

The initial screening process involved a review of titles and abstracts to identify potentially relevant studies. Full-text articles of the selected studies were then thoroughly analyzed for eligibility based on the inclusion and exclusion criteria. Data from the included studies were systematically extracted and organized using Microsoft Office Excel. The extracted variables included: Title and abstract, Materials and methods, Type of publication, Main results. Further, data were compiled into a structured table with the following information: author and year, study design, number of cases, age and gender of patients, tooth type, etiology, radiographic findings, diagnosis, treatment protocol (including irrigation, intracanal medicaments, and scaffold type), number of visits required, clinical signs and symptoms, root maturation, follow-up period, and treatment outcome (Table 2,3).

**Table 1. Search strategy used in the present study**

<b>Database</b>	<b>Search strategy</b>	<b>Result</b>
<b>Google scholar</b>	1. immature teeth' AND 'pulp revascularization' AND 'blood clot' AND 'apical closure.'	840
	2. immature teeth' AND 'pulp revascularization' OR 'regenerative endodontic' AND 'platelet-rich fibrin' AND 'root end formation'	1780
<b>PubMed</b>	1. immature teeth' AND 'pulp revascularization' OR 'pulpal regeneration' AND 'platelet-rich fibrin' AND 'root end formation.'	44
	2. immature teeth' OR 'immature dentition' AND 'pulp revascularization' OR 'regenerative endodontic' AND 'blood clot' OR 'platelet-rich fibrin' AND 'apical closure' OR 'root end formation.'	621

### **Critical appraisal**

All included studies were assessed for risk of bias using the Joanna Briggs Institute (JBI) critical appraisal checklists for case series and case reports (figure 1, 2). These checklists evaluate the methodological quality of studies by examining key factors such as clarity in patient selection, completeness of clinical and radiographic data, follow-up adequacy, and outcome reporting. Each study was critically analyzed to determine its reliability and potential sources of bias. The appraisal process ensured that only studies with sufficient methodological rigor contributed to the final synthesis of findings. The JBI critical appraisal checklists for case series and case reports are available at: <https://jbi.global/critical-appraisal-tools>.

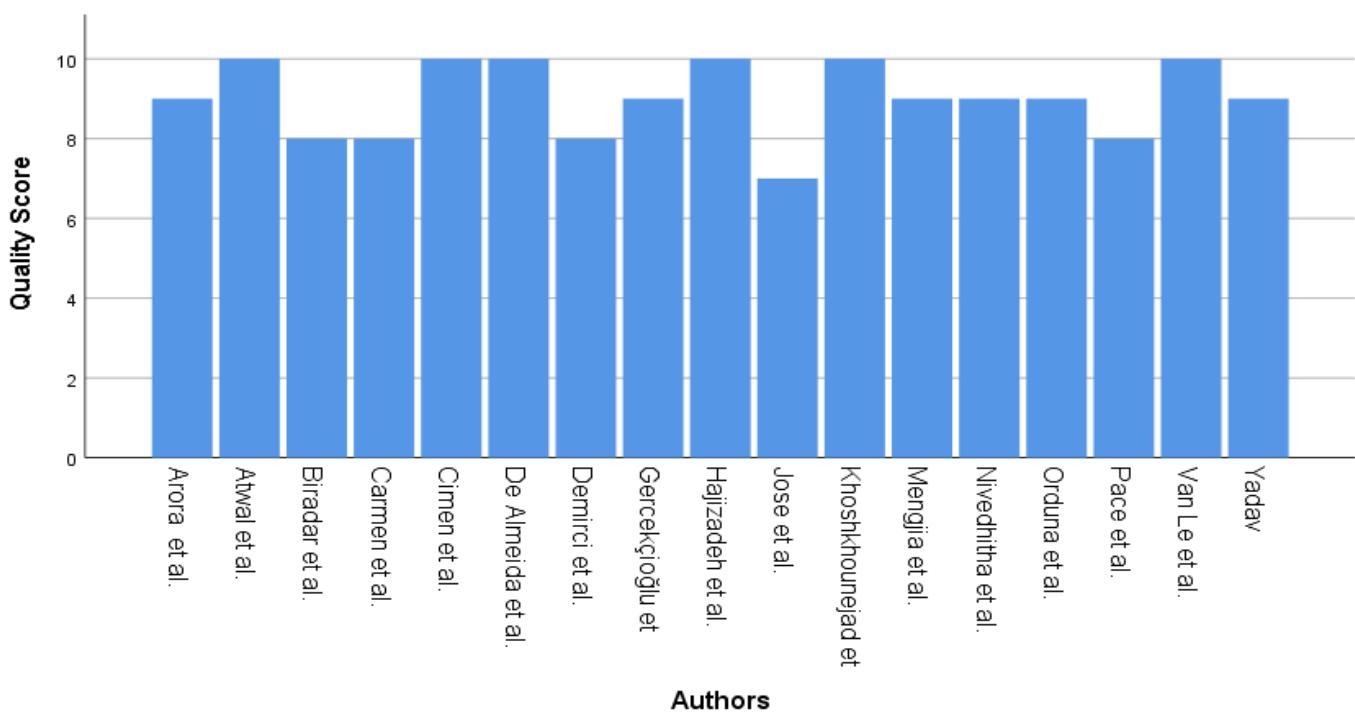


Figure 1. JBI critical appraisal scores of included case series studies

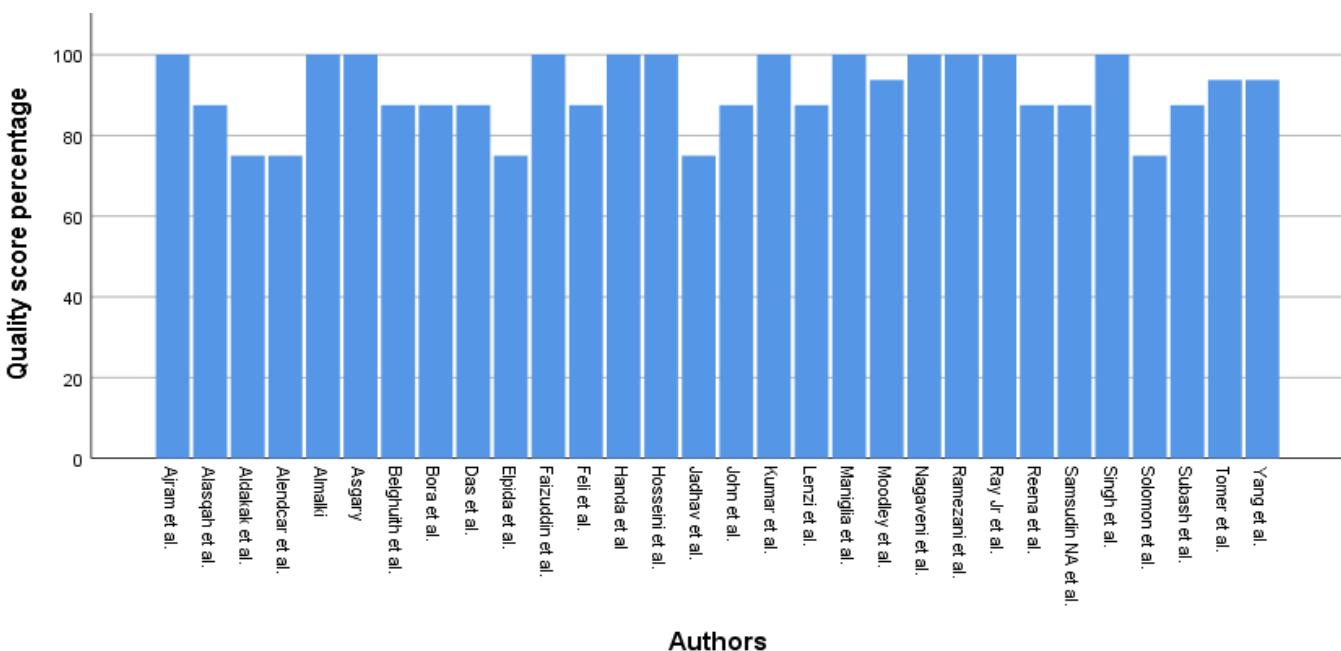


Figure 2. JBI critical appraisal scores of included case report studies

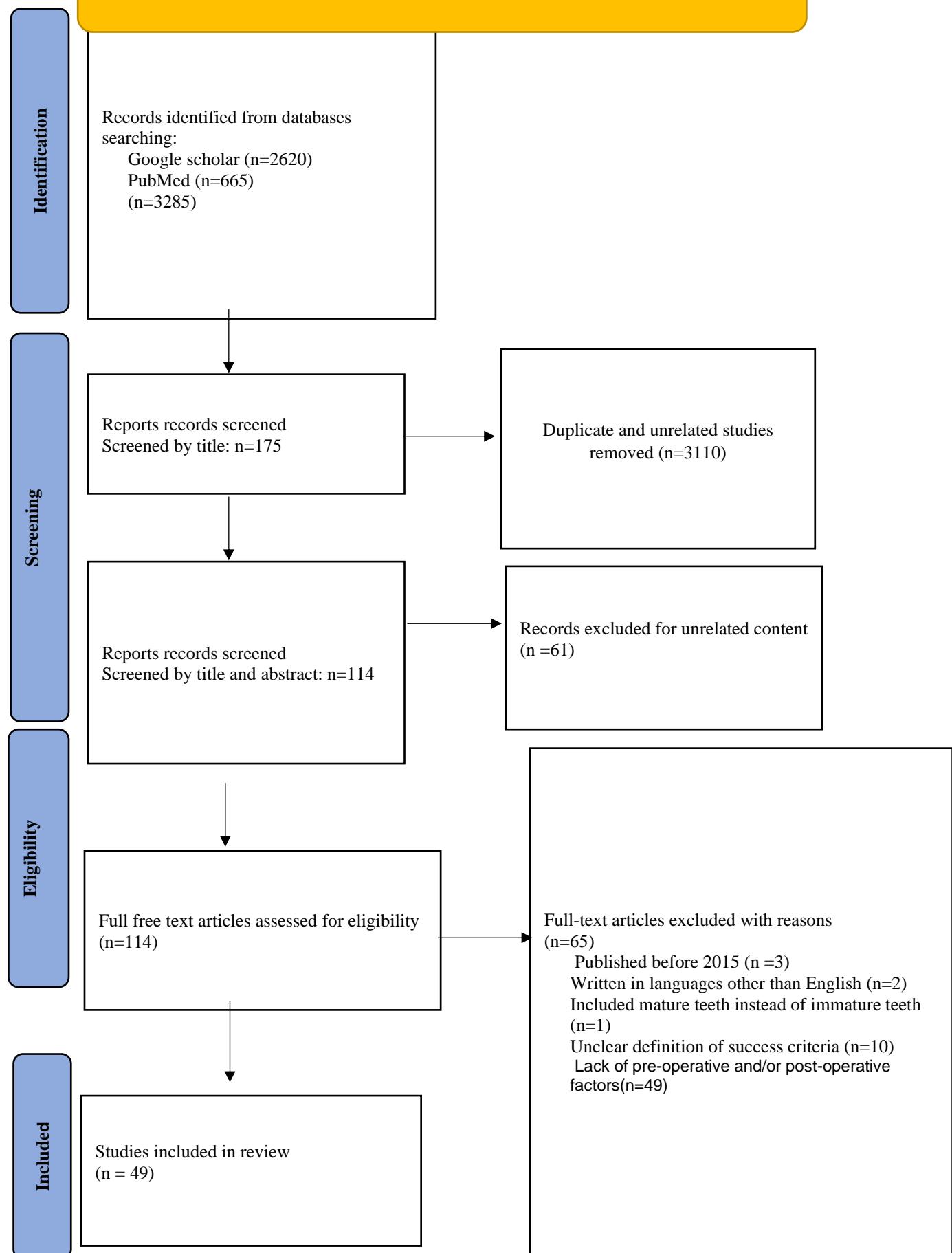
## Results

### *Study selection*

A total of 3,285 studies were initially retrieved using the selected keywords across the databases. After screening the titles, 3,110 studies were excluded due to duplication or irrelevance. An additional 61 studies

were removed after reviewing the abstracts for unrelated content. Following the application of inclusion and exclusion criteria, 114 articles were assessed for eligibility. Ultimately, 49 studies were included in this review. The flowchart detailing the selection process is presented in Flow chart 1.

**Flow chart 1: Search strategy used in this systematic review**



There were 92 cases of immature permanent necrotic teeth, categorized by gender, etiology (cause), and radiographic findings. In terms of gender distribution, the majority of cases involved males (47 cases, 51.1%), followed by females (36 cases, 39.1%), with 9 cases (9.8%) where gender was not specified. Regarding etiology (causes of the condition), trauma was the leading cause (47 cases, 51.1%), followed by caries (25 cases, 27.2%), and failed treatment (9 cases, 9.8%). Less common causes included fracture of the central cusp (6 cases, 6.5%), dens evaginatus (2 cases, 2.2%), and a single case of a worn-away central cusp (1.1%). The radiographic findings indicated that the majority of cases (81 cases, 88%) presented with periapical radiolucency, suggesting some form of periapical pathology, whereas only 11 cases (12%) showed no signs of periapical pathology. These findings highlight that trauma and caries are the most common causes of immature permanent necrotic teeth and that periapical radiolucency is the predominant radiographic feature in affected cases.

Out of all cases, 76 cases (82.6%) were classified as successful, meaning they were completely asymptomatic, showed healing of pre-apical radiolucency, and exhibited clear signs of root end maturation. Additionally, 13 cases (14.1%) were considered partially successful, as they remained asymptomatic with no signs of pathology in the pre-apical area, but they did not demonstrate root maturation. Finally, 3 cases (3.2%) were classified as failed, as they showed persistent clinical symptoms and a lack of both healing and root development. If success is defined as being completely asymptomatic and absence of pathology in the pre-apical area, the success rate reaches 96%.

#### ***Radiologic findings and diagnosis of successful RET cases***

Among the 76 successful cases, 10 cases showed no signs of pathology, while the remaining 66 cases exhibited pre-apical radiolucency, indicating initial periapical involvement that eventually healed post-treatment. The clinical diagnoses of these cases varied, reflecting a diverse range of pulpal and periapical conditions. The most commonly treated conditions included chronic apical abscess (17 cases) and symptomatic apical periodontitis (15 cases),

followed by pulp necrosis (13 cases) and chronic apical periodontitis (7 cases). Additionally, asymptomatic apical periodontitis (7 cases), acute apical abscess (6 cases), and irreversible pulpitis (5 cases) were successfully managed. Less frequently observed conditions included acute apical periodontitis (4 cases), symptomatic chronic periodontitis (1 case), and secondary acute apical periodontitis (1 case). These findings demonstrate that regenerative endodontic treatments were effective across a broad spectrum of endodontic diagnoses, particularly in cases with significant periapical pathology.

#### ***Irrigation Solutions and Intracanal Medicaments Used in Successful Cases***

The most commonly used irrigation protocol was a combination of NaOCl, saline, and EDTA, applied in 39 cases (51.3%), followed by NaOCl and EDTA in 17 cases (22.4%). Additionally, NaOCl with saline was used in 7 cases (9.2%), and EDTA with saline in 2 cases (2.6%). A few cases involved alternative irrigation solutions, such as HYBENX cleanser with NaOCl and sterile water in 1 case (1.3%), saline with CHX and NaOCl in 1 case (1.3%), NaOCl with distilled water in 1 case (1.3%), and NaOCl, EDTA, saline, and CHX in 1 case (1.3%). Meanwhile, 5 cases (6.6%) used only NaOCl, 1 case (1.3%) relied solely on saline, and 1 case (1.3%) had no irrigation type mentioned.

Among the successful cases, the most frequently used intracanal medicament was Triple Antibiotic Paste (TAP: metronidazole, ciprofloxacin, minocycline), which was applied in 42 cases (55.3%). Calcium hydroxide was the second most common medicament, used in 21 cases (27.6%), while Double Antibiotic Paste (DAP: ciprofloxacin and metronidazole) was used in 5 cases (6.6%). Other less commonly used medicaments included Calcium hydroxide combined with TAP in 2 cases (2.6%), Calcium hydroxide with Iodoform in 1 case (1.3%), and TAP containing metronidazole, ciprofloxacin, and amoxicillin in 1 case (1.3%). Additionally, 2% CHX gel combined with DAP was applied in 1 case (1.3%), and 3 cases (3.9%) did not specify the medicament used. The results show that NaOCl, EDTA, and saline (51.3%) was the most commonly used irrigation solution in successful cases, followed by NaOCl and EDTA alone (22.4%). Among medicaments, Triple Antibiotic Paste

(55.3%) was the most frequently used and effective, with Calcium Hydroxide (27.6%) also playing a significant role in successful outcomes. These findings highlight the importance of proper irrigation and medicament selection in regenerative endodontic procedures.

#### ***Capping Materials and Scaffolds Used in Successful Cases***

In the successful cases, Mineral Trioxide Aggregate (MTA) was the most commonly used capping material, applied in 54 cases (71.1%). Biodentine was the second most frequently used, appearing in 11 cases (14.5%), followed by Iroot BP Plus in 5 cases (6.6%) and Bioceramic materials in 3 cases (3.9%). Calcium-Enriched Mixture (CEM) cement was used in 1 case (1.3%), while 2 cases (2.6%) did not specify the capping material used.

Regarding scaffolds, Platelet-Rich Fibrin (PRF) was the most frequently utilized, supporting 40 cases (52.6%). Blood clot (BC) was used in 29 cases (38.2%), while a combination of Blood Clot and Platelet-Rich Fibrin was applied in 4 cases (5.3%). Additionally, Blood Clot and Platelet-Rich Plasma (PRP) were used together in 3 cases (3.9%), demonstrating the variation in scaffold selection across successful treatments.

**Table 2.** Preoperative factors of cases included in this study

N	Authors	Year	Type of study	Number of cases	Gender	Age	Tooth	Etiology	RAD findings	Diagnosis
1	Arora et al (12)	2020	Case series	9	Male	9	36	Caries	No signs of periapical pathology	Irreversible pulpitis
					Female	16	47	Caries	Periapical radiolucency	Chronic periapical abscess
					Female	14	47	Caries	Periapical radiolucency	Chronic apical periodontitis
					Female	7	36	Caries	Periapical radiolucency	Chronic apical periodontitis
					Male	8	36	Failed treatment	Periapical radiolucency	Chronic apical periodontitis
					Nm	Nm	Mandibular molar	Caries	No signs of periapical pathology	Pulp necrosis
					Nm	Nm	Mandibular molar	Caries	No signs of periapical pathology	Pulp necrosis
					Nm	Nm	Maxillary molar	Failed treatment	Periapical radiolucency	Pulp necrosis
					Nm	Nm	Mandibular molar	Caries	Periapical radiolucency	Pulp necrosis
2	Atwal et al (13)	2024	Case series	2	Male	25	22	Trauma	Periapical radiolucency	Chronic periapical abscess
3	Ray Jr et al (14)	2016	Case report	1	Male	11	21	Trauma	Periapical radiolucency	Asymptomatic apical periodontitis
4	Belghith et al (15)	2023	Case report	1	Male	9	21	Trauma	No signs of periapical pathology	Pulp necrosis
5	Bora et al (16)	2015	Case report	1	Male	11	31, 41	Trauma	Periapical radiolucency	Chronic apical abscess
6	Cimen et al (17)	2021	Case series	3	Male	8	11	Trauma	No signs of periapical pathology	Acute apical periodontitis
					Female	9	11	Trauma	Periapical radiolucency	Acute apical abscess
					Female	9	11, 21	Trauma	Periapical radiolucency	Chronic apical periodontitis
7	Almeida et al (18)	2023	Case series	2	Female	13	22	Nm	Periapical radiolucency	Chronic apical abscess
					Female	14	35	Failed treatment	No signs of periapical pathology	Acute apical periodontitis
8	Gercekçioğlu et al (19)	2021	Case series	2	Male	7	37	Caries	Periapical radiolucency	Pulp necrosis
					Male	22	45	Caries	Periapical radiolucency	Pulp necrosis
9	Handa et al (20)	2021	Case report	1	Female	28	21	Trauma	Periapical radiolucency	Chronic apical periodontitis
10	Jose et al (21)	2023	Case series	5	Female	10	Mandibular 2nd premolar	Caries	Periapical radiolucency	Acute apical periodontitis
					Female	8	11	Trauma	Periapical radiolucency	Pulp necrosis
					Female	8	21	Trauma	Periapical radiolucency	Pulp necrosis
					Male	8	11	Trauma	Periapical radiolucency	Pulp necrosis
					Male	8	21	Trauma	Periapical radiolucency	Pulp necrosis
11	Jose et al (22)	2021	Case Series	2	Female	17	21	Trauma	Periapical radiolucency	Symptomatic apical periodontitis
					Female	14	21	Trauma	Periapical radiolucency	Symptomatic apical periodontitis
12	Demirci et al (23)	2020	Case Series	3	Male	14	12	Trauma	Periapical radiolucency	Chronic apical periodontitis
					Male	14	11	Trauma	Periapical radiolucency	Chronic apical periodontitis
					Female	13	11	Trauma	Periapical radiolucency	Chronic apical periodontitis

Table 2. Preoperative factors of cases included in this study (continued)

N	Authors	Year	Type of study	Number of cases	Gender	Age	Tooth	Etiology	RAD findings	Diagnosis
13	Ajram et al (24)	2019	Case report	1	Female	7	36	Caries	Periapical radiolucency	Symptomatic apical periodontitis
14	Samsudin et al (25)	2021	Case report	1	Male	8	21	Trauma	Periapical radiolucency	Chronic apical periodontitis
15	Nagaveni et al (26)	2015	Case report	1	Male	10	11	Trauma	No signs of periapical pathology	Acute apical periodontitis
16	Orduna et al (27)	2017	Case series	3	Female	35	21	Trauma	Periapical radiolucency	Chronic apical abscess
					Nm	21	11	Trauma	Periapical radiolucency	Asymptomatic apical periodontitis
					Female	24	22	Failed treatment	Periapical radiolucency	Symptomatic apical periodontitis
17	Moodley et al (28)	2017	Case report	1	Male	10	11	Trauma	Periapical radiolucency	Chronic apical abscess
18	Reena et al (29)	2022	Case report	1	Male	18	11	Trauma	Periapical radiolucency	Chronic apical periodontitis
19	Singh et al (30)	2019	case report	1	Female	15	11	Trauma	Periapical radiolucency	Chronic apical periodontitis
20	Subash et al (31)	2016	case report	1	Female	13	37	Failed treatment	Periapical radiolucency	Symptomatic apical periodontitis
21	Tomer et al (32)	2019	case report	1	Male	16	21	Trauma	Periapical radiolucency	Asymptomatic apical periodontitis
22	Yang et al (33)	2022	case report	1	Male	26	47	central cusp that worn away	Periapical radiolucency	Chronic periapical periodontitis
23	Yadav (34)	2018	Case series	2	Female	34	11,21	Trauma	Periapical radiolucency	Symptomatic apical periodontitis
					Male	12	12	Trauma	Periapical radiolucency	Symptomatic apical periodontitis
24	Alasqah et al (35)	2020	case report	1	Male	8	Mandibular first molar	Caries	Periapical radiolucency	Asymptomatic apical periodontitis
25	Aldakak et al (36)	2016	case report	1	Female	11	42	Caries	No signs of periapical pathology	Pulp necrosis
26	Alendcar et al (37)	2022	case report	1	Male	6	21	Trauma	Periapical radiolucency	Chronic apical abscess
27	Almalki (38)	2024	case report	1	Female	7	46	Caries	Periapical radiolucency	Asymptomatic apical periodontitis
28	Asgary (39)	2024	case report	1	Female	7	21	Trauma	Periapical radiolucency	Pulp necrosis
29	Carmen et al (40)	2017	Case series	4	Nm	8	46	Caries	Periapical radiolucency	Irreversible pulpitis
					Nm	8.5	21	Trauma	Periapical radiolucency	Pulp necrosis
					Nm	6.5	36	Caries	Periapical radiolucency	Irreversible pulpitis
					Nm	8	36	Caries	Periapical radiolucency	Pulp necrosis
30	Das et al (41)	2023	Case report	1	Male	7	46	Caries	Periapical radiolucency	Irreversible pulpitis
31	Faizuddin et al (42)	2015	Case report	1	Male	14	11, 12	Trauma	Periapical radiolucency	Symptomatic chronic periodontitis
32	Feli et al (43)	2024	Case report	1	Female	9	30	Failed treatment	Periapical radiolucency	Secondary acute apical periodontitis

Table 2. Preoperative factors of cases included in this study (continued)

N	Authors	Year	Type of study	Number of cases	Gender	Age	Tooth	Etiology	RAD findings	Diagnosis
33	Hajizadeh et al (44)	2019	Case series	3	Male	7	36	Caries	Periapical radiolucency	Symptomatic apical periodontitis
					Male	9	46	Caries	Periapical radiolucency	Chronic apical abscess
					Male	8	46	Caries	No signs of periapical pathology	Acute apical periodontitis
34	Hosseini et al (45)	2023	Case report	1	Male	11	20	Caries	Periapical radiolucency	Symptomatic apical periodontitis
35	Jadhav et al (46)	2015	Case report	1	Male	16	21	Nm	Periapical radiolucency	Chronic apical abscess
36	John et al (47)	2019	Case report	1	Male	10	21	Trauma	No signs of periapical pathology	Pulp necrosis
37	Khoshkhounnejad et al (48)	2015	Case series	2	Male	16	21	Trauma	Periapical radiolucency	Asymptomatic apical periodontitis
					Female	17	45	Caries	Periapical radiolucency	Chronic apical abscess
38	Kumar et al (49)	2023	Case report	1	Female	8,4	11	Trauma	No signs of periapical pathology	Pulp necrosis
39	Lenzi et al (50)	2022	Case report	1	Female	44	21	Failed treatment	Periapical radiolucency	Acute apical abscess
40	Manigli et al (51)	2020	Case report	1	Female	7	21	Trauma	Periapical radiolucency	Acute apical abscess
41	Elpida et al (52)	2015	Case report	1	Male	14	11	Trauma	Periapical radiolucency	Symptomatic apical periodontitis
42	Nagaveni et al (53)	2016	Case report	1	Male	11	11	Trauma	Periapical radiolucency	Symptomatic apical periodontitis
43	Biradar et al (54)	2023	Case series	3	Female	11	11,12	Failed treatment	Periapical radiolucency	Chronic apical abscess
					Male	9	21	Trauma	Periapical radiolucency	Acute apical abscess
					Male	13	11,21	Trauma	Periapical radiolucency	Irreversible pulpitis
44	Nivedhitha et al (55)	2020	Case series	2	Male	23	12,12	Trauma	Periapical radiolucency	Symptomatic apical periodontitis
					Male	21	21	Trauma	Periapical radiolucency	Chronic apical abscess
45	Pace et al (56)	2021	Case series	2	Male	15	15	Failed treatment	Periapical radiolucency	Symptomatic apical periodontitis
					Male	8	36	Caries	Periapical radiolucency	Asymptomatic apical periodontitis
46	Ramezani et al (57)	2020	Case report	1	Female	8	46	Caries	Periapical radiolucency	Symptomatic apical periodontitis
47	Solomon et al (58)	2015	Case report	1	Male	15	11	Trauma	Periapical radiolucency	Symptomatic apical periodontitis
48	Van Le et al (59)	2023	Case series	2	Male	12	35	Dens evaginatus	Periapical radiolucency	Chronic apical abscess
					Female	12	35	Dens evaginatus	Periapical radiolucency	Symptomatic apical periodontitis
49	Mengjia et al (60)	2024	Case series	10	Female	10	45	Fracture of central cusp	Periapical radiolucency	Acute apical abscess
					Female	7	21	Trauma	Periapical radiolucency	Chronic apical abscess
					Male	10	35	Fracture of central cusp	Periapical radiolucency	Chronic apical abscess
					Male	11	35	Fracture of central cusp	Periapical radiolucency	Chronic apical abscess
					Male	12	22	Trauma	Periapical radiolucency	Chronic apical abscess
					Male	9	35	Fracture of central cusp	Periapical radiolucency	Chronic apical abscess
					Female	8	11	Trauma	Periapical radiolucency	Chronic apical abscess
					Male	10	10	Trauma	Periapical radiolucency	Chronic apical abscess
					Female	13	13	Fracture of central cusp	Periapical radiolucency	Acute apical periodontitis
					Female	11	45	Fracture of central cusp	Periapical radiolucency	Acute apical abscess

Table 3. Postoperative factors of cases included in this study

N	Study	Irrigation type	Type of medicament	Number of visits	Capping material	Scaffolds	Sign and symptoms	Root maturation	Follow-up period	Result
1	Arora et al.	3% NaOCL Saline and EDTA	TAP	2	MTA	PRF	Pre-apical radiolucency was healed and asymptomatic	Complete closure of the root end and increased root length.	6 months, 1, 2, 3 and 5 years	Success
		3% NaOCL Saline and EDTA	TAP	2	MTA	PRF	Asymptomatic	Complete closure of the root ends with increase in thickness of root dentin	3 years and 5 years	Success
		3% NaOCL Saline and EDTA	TAP	2	MTA	PRF	Asymptomatic	Complete healing and closure of apex	2 years	Success
		3% NaOCL Saline and EDTA	TAP	2	MTA	PRF	Asymptomatic	Root end closure and increased distal root width	1-year, 2-year, and 5-year	Success
		3% NaOCL Saline and EDTA	TAP	2	MTA	PRF	Asymptomatic	Complete healing and closure of apex	5 years	Success
		3% NaOCL Saline and EDTA	TAP	2	MTA	PRF	Asymptomatic	Satisfactory healing and closure of apex	3-month, 6-month, and 1-year	Success
		3% NaOCL Saline and EDTA	TAP	2	MTA	PRF	Asymptomatic	Satisfactory healing and closure of apex	3-month, 6-month, and 1-year	Success
		3% NaOCL Saline and EDTA	TAP	2	MTA	PRF	Asymptomatic	Satisfactory healing and closure of apex	1-year, 2-year, and 5-year	Success
		3% NaOCL Saline and EDTA	TAP	2	MTA	PRF	Asymptomatic	Satisfactory healing and closure of apex	1-year, 2-year, and 5-year	Success
2	Atwal et al.	1.5% NaOCL EDTA	TAP	2	Biodentine	PRF	Pre-apical radiolucency was healed and asymptomatic	Partially thickening of dentinal walls	3, 6 months, and yearly up to 3 years	Success
		1.5% NaOCL 17% EDTA	TAP	2	MTA	PRF	Pre-apical radiolucency was healed and asymptomatic	Root lengthening and thickening of dentinal walls were not observed	8 years	Partially success
3	Ray Jr et al.	0.5% NaOCL 17% EDTA	DAP	2	MTA	PRF	Asymptomatic	Increase in root length	12, 24 and 36 month	Success
4	Belghith et al.	2.5% NaOCL EDTA, saline	Ca(OH) <sub>2</sub>	2	MTA	PRF	Asymptomatic	Apical closure, root lengthening and dentinal wall thickening	6 and 12 month	Success
5	Bora et al.	1.5% NaOCL saline	TAP	2	MTA	PRF	Pre-apical radiolucency was healed and asymptomatic	Thickening of the dentinal walls, root lengthening, and apical closure	1, 3, 6, 9 months, and 1-year	Success
6	Cimen et al.	1.5% NaOCL saline, 17%EDTA	DAP	2	Biodentin	PRF	Asymptomatic	Apical closure	3, 12 and 18 month	Success
		1.5% NaOCL saline, 17%EDTA	DAP	2	Biodentin	PRF	Pre-apical radiolucency was healed and asymptomatic	Apical closure has not been observed	12 and 18 month	Partially success
		1.5% NaOCL saline, 17%EDTA	DAP	2	Biodentin	PRF	Pre-apical radiolucency was healed and asymptomatic	Root development was completed in both teeth	3, 6, 12, 18 and 24 month	Success

Table 3. Postoperative factors of cases included in this study (continued)

N	Study	Irrigation type	Type of medicament	Number of visits	Capping material	Scaffolds	Sign and symptoms	Root maturation	Follow-up period	Result
7	De Almeida et al.	3% NaOCL 17% EDTA, Saline 2% CHX	Ca(OH) <sub>2</sub>	2	Bioceramic material	BC	Pre-apical radiolucency was healed and asymptomatic	Increased thickness of radicular wall	1-year, 2-year, and 4-year	Success
		3% NaOCL 17% EDTA, Saline 2% CHX	Ca(OH) <sub>2</sub>	2	Bioceramic material	BC	Pre-apical radiolucency was healed and asymptomatic	Increased thickness of the radicular wall	1, 6, 12 months, and 2-year	Success
8	Gerekçioğlu et al.	1% NaOCL and 2% CHX	No medicament then TAP	10	MTA Plus	BC	Pre-apical radiolucency was healed and asymptomatic	Apical closure has not been observed	1-year	Partially success
		Distilled water 1% NaOCL, EDTA	TAP	2	MTA Plus	PRF	Pre-apical radiolucency was healed and asymptomatic	Apical closure has not been observed	6 months	Partially success
9	Handa et al.	1.5% NaOCL 17% EDTA	TAP	2	MTA	BC+PRF	Asymptomatic	Thickening of root dentinal walls and further root development	6 months, 1 year, and 1.5 year	Success
10	Jose et al.	1.5 % NaOCL Saline, EDTA	TAP	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Normal maturation of root/thickening of dentinal walls and root lengthening	12-month and 18-month	Success
		1.5 % NaOCL Saline, EDTA	TAP	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Normal maturation of root/thickening of dentinal walls and root lengthening	1-year	Success
		1.5 % NaOCL Saline, EDTA	TAP	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Normal maturation of root/thickening of dentinal walls and root lengthening	1-year	Success
		1.5 % NaOCL Saline, EDTA	TAP	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	No radiographic sign of root development	1-year	Partially success
		1.5 % NaOCL Saline, EDTA	TAP	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Normal maturation of root/thickening of dentinal walls and root lengthening	1-year	Partially success
11	Jose et al.	17% EDTA, saline	TAP	2	Biodentine	PRF	Pre-apical radiolucency was healed and asymptomatic	Thickening of the dentinal walls and apical closure	1, 6, and 12 months	Success
		17% EDTA, saline	TAP	2	Biodentine	PRF	Pre-apical radiolucency was healed and asymptomatic	Thickening of the dentinal walls and apical closure	1, 6, and 12 months	Success
12	Demirci et al.	1.5% NaOCL 17% EDTA	TAP	2	MTA	BC + PRF	Pre-apical radiolucency was healed and asymptomatic	There were no obvious changes in root wall thickness and/or root length	36 months	Partially success
		1.5% NaOCL 17% EDTA	TAP	2	MTA	BC + PRF	Pre-apical radiolucency was healed and asymptomatic	There were no obvious changes in root wall thickness and/or root length	36 months	Partially success
		1.5% NaOCL 17% EDTA	TAP	2	MTA	BC + PRF	Pre-apical radiolucency was healed and asymptomatic	There were no obvious changes in root wall thickness and/or root length	36 months	Partially success

Table 3. Postoperative factors of cases included in this study (continued)

N	Study	Irrigation type	Type of medicament	Number of visits	Capping material	Scaffolds	Sign and symptoms	Root maturation	Follow-up period	Result
13	Ajram et al.	2.5% NaOCL 20% EDTA, saline	Ca(OH)2	2	MM-MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Apical closure and significant increase in root length and dentin thickness	3, 9, 12 and 24 months	Success
14	Samsudin NA et al.	0.9% NaOCL 17% EDTA	DAP	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Apical closure at 12 months	1, 3, 6, 9 and 12 months	Success
15	Nagavni Nagavni et al.	5.25% NaOCL	TAP	2	White MTA	PRF	Asymptomatic	Root end development, thick dentinal walls	One, three, six, nine, and 12 months	Success
16	Orduna et al.	5.25% NaOCL saline	TAP	2	MTA	BC and PRP	Pre-apical radiolucency was healed and asymptomatic	A slight invagination of bone inside the canal was observed	1,2,6,12,24,36 and 50 months	Success
		5.25% NaOCL saline	TAP	2	MTA	BC and PRP	Pre-apical radiolucency was healed and asymptomatic	A slight increase of root length was also observed	6 months and 5 years	Success
		5.25% NaOCL saline	TAP	2	MTA	BC and PRP	Pre-apical radiolucency was healed and asymptomatic	Calcified tissue over the entire canal wall especially in the apical third	48 months	Success
17	Moodley et al.	1.5% NaOCL 17%EDTA	TAP	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Increased width of root walls and closure of the apex was noted	2 and 5 months	Success
18	Reena et al.	2.5% NaOCL saline, 17 % EDTA	Ca(OH) <sub>2</sub>	2	Biodentine	PRF	Pre-apical radiolucency was healed and asymptomatic	Apical plug formed	24 months	Success
19	Singh et al.	1.5%NaOCL Distilled water	Ca(OH) <sub>2</sub> and iodoform	3	Biodentine	BC PRF	Pre-apical radiolucency was healed and asymptomatic	Continued thickening of the dentinal walls and apical closure	1 week, 1 month and every 3 months	Success
20	Subash et al.	5.25% NaOCL Saline	TAP	2	Biodentine	PRF	Pre-apical radiolucency was healed and asymptomatic	Thickening of the dentinal walls, root lengthening with apical closure	3, 6, 9 and 12 months	Success

Table 3. Postoperative factors of cases included in this study (continued)

N	Study	Irrigation type	Type of medicament	Number of visits	Capping material	Scaffolds	Sign and symptoms	Root maturation	Follow-up period	Result
21	Tomer et al.	3% NaOCL 17% EDTA	TAP	2	Biodentine	PRF	Pre-apical radiolucency was healed and asymptomatic	Thickening of dentinal walls, root lengthening with apical closure	3,6,12 months	Success
22	Yang et al.	3% NaOCL 17% EDTA	TAP(cefaclor, ciprofloxacin, metronidazole)	2	Iroot BP	BC and gelatine sponge	Pre-apical radiolucency was healed and asymptomatic	The canal walls did not thicken, and the apex also did not appear to have closed	6,12,24 and 36 months	Partially success
23	Yadav	NaOCL, EDTA	TAP	3	MTA	BC and PRF	Pre-apical radiolucency was healed and asymptomatic	Narrowing of apical foramen	6 and 12 months	Success
		NaOCL, EDTA	TAP	3	MTA	BC and PRF	Pre-apical radiolucency was healed and asymptomatic	Narrowing of apical foramen	6 and 12 months	Success
24	Alasqah et al.	1.5% NaOCL 17%EDTA	Ca(OH) <sub>2</sub> /TAP	3	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Increased root thickness and length and apical closure	3, 6, 12, and 24 months	Success
25	Aldakak et al.	5.25% NaOCL 17%EDTA Saline, 2%CHX	Nm	1	Biodentine	BC	Pre-apical radiolucency was healed and asymptomatic	Complete root maturation	6, 12, and 24 months	Success
26	Alendca et al.	1.5% NaOCL 17%EDTA	Ca(OH) <sub>2</sub>	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Thickening of canal walls and continued root maturation	6,12,18 and 36 months	Success
27	Almalki	1.5% NaOCL 17% EDTA	TAP	2	White MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Apical closure, increased root length, increased dentin thickness	6, 12, and 24 months	Success
28	Asgary	NaOCL EDTA	TAP	2	CEM	BC	Pre-apical radiolucency was healed and asymptomatic	Complete tooth maturation	6 months and 7 years	Success

Table 3. Postoperative factors of cases included in this study (continued)

N	Study	Irrigation type	Type of medicament	Number of visits	Capping material	Scaffolds	Sign and symptoms	Root maturation	Follow-up period	Result
29	Carmen et al.	5% NaOCL	TAP	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Increased dentinal wall thickness and an almost closed apical foramen	6 and 12 months	Success
		5% NaOCL	TAP	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	An appreciable increase in root length and the apex has closed.	3,7 month, 1 year and 7 months	Success
		5% NaOCL	TAP	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	The walls of the root canal have thickened.	8 months	Success
		5% NaOCL	TAP	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	The walls of the root canal had thickened.	9 months	Success
30	Das et al.	1.5% NaOCL Saline, 17% EDTA	TAP	2	White MTA	PRF	Asymptomatic	Increase in the root apex formation	6 months	Success
31	Faizuddin et al.	5.25% NaOCL Saline, 0.2% CHX	TAP	3	MTA	PRF	Pre-apical radiolucency was healed and asymptomatic	Initiation of root end closure	3, 6, 9, 12 and 14 months	Success
32	Felli et al.	1.5% NaOCL 17% EDTA	Ca(OH) <sub>2</sub>	2	MTA	PRF	Pre-apical radiolucency was healed and asymptomatic	A slight increase in the thickness of the root walls & increased root length	6 months, 1 year, and 2 years	Success
33	Hajizadeh et al.	2.5% NaOCL Saline, 17%EDTA	Nm	1	MTA	BC	Asymptomatic	Apical closure after 12 months	3 and 12 months	Success
		2.5% NaOCL Saline, 17%EDTA	TAP	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Apical closure	3, 6 and 12 months	Success
		2.5% NaOCL Saline, 17%EDTA	TAP	2	MTA	BC	Asymptomatic	Apical closure	1, 3, 6 and 12 months	Success
34	Hosseini et al.	1.5% NaOCL Saline, 17% EDTA	Ca(OH) <sub>2</sub>	3	MTA	PRF	Pre-apical radiolucency was healed and asymptomatic	Apical closure	3, 6, 12, and 24 months	Success
35	Jadhav et al.	Nm	TAP	2	MTA	PRF	Pre-apical radiolucency was healed and asymptomatic	Apical closure	12 and 18 months	Success

Table 3. Postoperative factors of cases included in this study (continued)

N	Study	Irrigation type	Type of medicament	Number of visits	Capping material	Scaffolds	Sign and symptoms	Root maturation	Follow-up period	Result
36	John et al.	5.25% NaOCL Saline	Ca(OH) <sub>2</sub> / TAP	3	MTA	PRF	Asymptomatic	Apical closure and dentinal wall thickening	6 months and at 1 year	Success
37	Khoshkhounnejad et al.	5.25% NaOCL 0.2%CHX	TAP(doxycycline ciprofloxacin, metronidazole,)	2	MTA	BC	Recurrence of pus discharge	No evidence of thickening of the canal walls or continuation of root development	3,6 months	Failed
		1.5% NaOCL 17% EDTA	TAP(doxycycline ciprofloxacin, metronidazole)	2	Biodentine	BC	Asymptomatic	No evidence of thickening of the canal walls or root development	3,6 months and one year	Partially success
38	Kumar et al.	0.09% saline	TAP	2	MTA	PRF	Asymptomatic	Increased root lengthening, closure of apex, increased dentinal thickness	6,9,12 months	Success
39	Lenzi et al.	1% NaOCL 17% EDTA	DAP	2	Bioceramic	BC	Pre-apical radiolucency was healed and asymptomatic	Newly formed bone visible at the very apical part of the apical foramen	8 and 34 months	Success
40	Maniglia et al.	2.5% NaOCL 17% EDTA, Saline	2% CHX gel/DAP (metronidazole, ciprofloxacin)	3	White MTA	BC	Asymptomatic	Progression of root development and apical closure	1,5 and 12 years	Success
41	Elpida et al.	2.5% NaOCL 17% EDTA	TAP(amoxicillin , ciprofloxacin, metronidazole)		Membrane barrier, MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Apical closure	Yearly 3 years	Success
42	Nagaveni et al.	5.25% NaOCL Saline	TAP	2	MTA	PRF	Asymptomatic	Apical closure	One, three, six, nine and 12 months	Success
43	Biradar et al.	1.5% NaOCL Saline, 17% EDTA	TAP	2	Nm	PRF	Pre-apical radiolucency was healed and asymptomatic	There was no significant increase in the thickness of the wall of the root	6 or 12 months	Partially success
		1.5% NaOCL Saline, 17% EDTA	TAP	2	Nm	PRF	Pre-apical radiolucency was healed and asymptomatic	Partially apical closure	6 months	Success
		1.5% NaOCL Saline, 17% EDTA	TAP	2	Nm	PRF	Pre-apical radiolucency was healed and asymptomatic	Partially apical closure	3 months	Success

Table 3. Postoperative factors of cases included in this study (continued)

N	Study	Irrigation type	Type of medicament	Number of visits	Capping material	Scaffolds	Sign and symptoms	Root maturation	Follow-up period	Result
44	Nivedhitha et al.	1.5% NaOCL Saline , 17%EDTA	Ca(OH) <sub>2</sub>	2	MTA	BC PRF	Pre-apical radiolucency was healed and asymptomatic	Root dentin thickness	12 months	Success
		1.5% NaOCL Saline, 17%EDTA	Ca(OH) <sub>2</sub>	2	MTA	BC PRF	Pre-apical radiolucency was healed and asymptomatic	Increased root dentin thickness	12 months	Success
45	Pace et al.	2.5% of NaOCL HYBENX® cleanser Sterile water	Nm	1	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	No root development	6 and 12 months	Partially success
		2.5% of NaOCL HYBENX® cleanser Sterile water	Nm	1	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Partial apical closure of both roots	6 and 12 months	Success
46	Ramezani et al.	1.5% NaOCL Saline, 17% EDTA	Ca(OH) <sub>2</sub>	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Root maturation and closing of the apical foramen	3,6 months 1 year	Success
47	Solomon et al.	Saline, 0.5%NaOCL 2% CHX	TAP	2	White MTA	PRF	Pre-apical radiolucency was healed and asymptomatic	Initiation of the root end closure	1, 3, 6, 1 year, and 18 months	Success
48	Van Le et al.	1.5% NaOCL EDTA 17%	Ca(OH) <sub>2</sub>	2	Collacote with proroot MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Significant increase in root length and complete apex closure	6, 12, and 18 months	Success
		1.5% NaOCL EDTA 17%	Ca(OH) <sub>2</sub>	2	Biodentine	BC	Pre-apical radiolucency was healed and asymptomatic	Significant complete apex closure	6, 12, and 18 months	Success

**Table 3. Postoperative factors of cases included in this study (continued)**

N	Study	Irrigation type	Type of medicament	Number of visits	Capping material	Scaffolds	Sign and symptoms	Root maturation	Follow-up period	Result
49	Mengjia et al.	1.5% NaOCL Saline, 17% EDTA	Ca(OH) <sub>2</sub>	2	Biomembrane/i root BP Plus	BC	Pre-apical radiolucency was healed and asymptomatic	Increase in length and thickness	12 to 48 months	Success
		1.5% NaOCL Saline, 17% EDTA	Ca(OH) <sub>2</sub>	2	Biomembrane/i root BP Plus	PRF	Pre-apical radiolucency had not disappeared	No obvious change	12 to 48 months	Failed
		1.5% NaOCL Saline, 17% EDTA	Ca(OH) <sub>2</sub>	2	Biomembrane/ MTA	PRF	Pre-apical radiolucency was healed and asymptomatic	Increase in length and thickness	12 to 48 months	Success
		1.5% NaOCL Saline, 17% EDTA	Ca(OH) <sub>2</sub>	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Increase in length and thickness	12 to 48 months	Success
		1.5% NaOCL Saline, 17% EDTA	Ca(OH) <sub>2</sub>	2	Iroot BP Plus	PRF	Pre-apical radiolucency was healed and asymptomatic	Increase in length and thickness	12 to 48 months	Success
		1.5% NaOCL Saline, 17% EDTA	Ca(OH) <sub>2</sub>	2	Iroot BP Plus	PRF	Pre-apical radiolucency was healed and asymptomatic	Increase in length and thickness	12 to 48 months	Success
		1.5% NaOCL Saline, 17% EDTA	Ca(OH) <sub>2</sub>	2	Biomembrane iroot BP Plus	PRF	Pre-apical radiolucency was healed and asymptomatic	Increase in length and thickness	12 to 48 months	Success
		1.5% NaOCL Saline, 17% EDTA	Ca(OH) <sub>2</sub>	2	Biomembrane iroot BP Plus	PRF	Pre-apical radiolucency was healed and asymptomatic	Increase in length and thickness	12 to 48 months	Success
		1.5% NaOCL Saline, 17% EDTA	Ca(OH) <sub>2</sub>	2	MTA	BC	Pre-apical radiolucency decreased at first and then increased	Increase in length, but no obvious change in thickness	12 to 48 months	Failed
		1.5% NaOCL Saline, 17% EDTA	Ca(OH) <sub>2</sub>	2	MTA	BC	Pre-apical radiolucency was healed and asymptomatic	Increase in length and thickness	12 to 48 months	Success

NaOCL: Sodium hypochlorite, EDTA: Ethylene Diamine Tetra Acetic acid, CHX: Chlorhexidine digluconate, TAP: Triple antibiotic paste (metronidazole, ciprofloxacin, minocycline), DAP: Double antibiotic paste (ciprofloxacin and metronidazole), Ca(OH)<sub>2</sub>: Calcium Hydroxide, MTA: Mineral Trioxide Aggregate, PRF: Platelet-Rich Fibrin, PRP: Platelet-Rich Plasma, BC: Blood clot, MM: Micro-Mega, Nm: Not mentioned

## Discussion

Regenerative endodontic treatment (RET) has emerged as a promising approach for managing immature necrotic teeth by promoting continued root development and periapical healing. Unlike traditional apexification techniques, which create an artificial barrier but do not facilitate further root growth, RET utilizes biologically active materials to stimulate tissue regeneration. The findings of this systematic review demonstrate a high success rate of 82.6%, with most cases achieving complete healing, resolution of pre-apical radiolucency, and root maturation and if success is defined as the absence of pathology in the pre-apical area, the success rate reaches 96%. The effectiveness of RET appears to be influenced by factors such as the choice of irrigation solutions, intracanal medicaments, scaffold materials, and capping agents, all of which play a crucial role in supporting cell viability, differentiation, and tissue repair. These findings align with previous systematic reviews supporting the high success rates of RET. Alghamdi and Alsulaimani reported a 96% healing rate of periapical pathology in successful RET cases, with 45% of cases showing root development, highlighting the potential of RET to promote functional tooth maturation (61). Similarly, Jiahua Li et al, in their meta-analysis of 27 randomized controlled trials, found a 95.6% success rate and a 96.2% asymptomatic rate, reinforcing the reliability of RET in treating necrotic immature permanent teeth (62). The success of RET in eliminating clinical symptoms is further supported by Kharchi et al, who reviewed five studies and found that infection management led to complete symptom resolution and tooth survival in all cases. Beyond infection control and periapical healing, improvements in root development have been observed, which directly impact the long-term functionality and survival of treated teeth (63). Shaik et al found that periapical pathology resolution was consistently reported in almost 100% of studies included in their meta-analysis, while apical closure was observed in 76% to 91% of cases. Additionally, success rates for root lengthening and dentin thickening ranged from 80% to 94%, demonstrating that RET contributes to significant structural improvements (64). Sabeti et al further emphasized that PRP and PRF scaffolds showed superior success rates in achieving root lengthening within 6 to 12 months compared to traditional blood clot scaffolds, suggesting that scaffold selection plays a

critical role in treatment outcomes (65). Clinical trials further support these findings, demonstrating the regenerative potential of RET. A study by Ragab et al evaluated the treatment of traumatized necrotic immature permanent anterior teeth and found a reduction in periapical radiolucency across all cases. Additionally, 72% of cases (8 out of 11) developed calcific barriers, while 27% (3 cases) showed no signs of calcification, indicating some variability in outcomes (9). Another randomized clinical trial by Zhang and Sheng assessed the effectiveness of RET in 54 non-vital immature teeth. At 6-month and 12-month follow-ups, 92.6% of patients (25 out of 27) showed favorable clinical and radiographic outcomes, confirming that RET is a conservative and effective method for promoting maturogenesis in non-vital teeth (5). Despite the high success rates observed in RET, this systematic review has several limitations that should be acknowledged. One major limitation is the reliance on case series and case reports, which lack the methodological rigor of randomized controlled trials (RCTs). The absence of large-scale clinical trials limits the generalizability of the findings. Additionally, variability in treatment protocols, including differences in irrigation solutions, intracanal medicaments, scaffold materials, and capping agents, makes it challenging to establish a standardized protocol for RET. Another limitation is the inconsistency in follow-up durations across studies, which prevents a clear understanding of the long-term efficacy and stability of RET outcomes. While most studies reported symptom resolution and periapical healing, differences in radiographic interpretation and clinical evaluation criteria may have introduced bias in assessing treatment success. Furthermore, the lack of control groups in many studies limits the ability to compare RET outcomes with other treatment modalities, such as apexification or conventional endodontic therapy. Additionally, patient-specific factors such as systemic conditions and immune responses were not consistently reported, making it difficult to determine how these variables influence treatment outcomes. Potential publication bias is also a concern, as studies with positive results are more likely to be published, potentially overestimating the overall success rate of RET while underreporting failures or complications. To address these limitations, future research should focus on well-designed randomized controlled trials with

standardized treatment protocols and extended follow-up periods. Comparative studies evaluating RET alongside traditional treatment approaches will provide a clearer understanding of its effectiveness. Moreover, incorporating objective radiographic and histological assessments will enhance the reliability of outcome measurements, ultimately contributing to the refinement and optimization of regenerative endodontic procedures.

## Conclusion

The findings of this study and systematic review collectively emphasize the high effectiveness of regenerative endodontic treatment (RET) in managing immature permanent necrotic teeth. Trauma emerged as the leading cause of the condition, followed by caries and failed treatments. RET demonstrated significant clinical and radiographic success, with 82.6% of cases achieving complete healing and root maturation, while a smaller percentage showed partial success or failure due to persistent symptoms. A variety of clinical diagnoses, including chronic and symptomatic apical abscesses, pulp necrosis, and apical periodontitis, were successfully managed through RET. The selection of irrigation solutions, intracanal medicaments, capping materials, and scaffolds played a crucial role in treatment success. The most frequently used irrigation protocol included NaOCl, saline, and EDTA (51.3%), while Triple Antibiotic Paste (TAP) (55.3%) and Calcium Hydroxide (27.6%) were the preferred medicaments. Among the capping materials, MTA (71.1%) was most commonly used, followed by Biodentine (14.5%) and Iroot BP Plus (6.6%). As for scaffolds, Platelet-Rich Fibrin (52.6%) and Blood Clot (38.2%) were the most frequently utilized, supporting root maturation and healing. With a high success rate and predictable outcomes, RET proves to be a reliable approach for preserving and promoting the development of immature necrotic teeth, particularly in cases with periapical pathology. However, variations in success rates highlight the need for further research to refine treatment protocols, optimize scaffold selection, enhance medicament formulations, and improve long-term outcomes. Future studies should focus on standardizing follow-up durations and exploring novel materials to increase the predictability and efficacy of regenerative endodontic procedures.

### Conflicts of interest

None.

### Author contribution

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### Consent

Not available.

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