

# Clinical Efficacy of Placental Derived Membranes in Treatment of Gingival Recession- A Systematic Review

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## Abstract

**Scientific rationale for the study:** Gingival recession is a condition causing functional and esthetic disturbances and has a high prevalence rate. A wide range of surgical techniques and membranes have been proposed through the decades for recession coverage. Amnion/ chorion membranes are rich in type I, IV, V, and VI collagen, proteoglycans, laminin, and fibronectin, demonstrating properties of wound protection, pain reduction, and effect on epithelialization and being bacteriostatic in nature. The available evidence suggests that Coronally Advanced Flap (CAF) combined with amnion/chorion membranes has significant effect on gingival recession, gingival phenotype, gain in clinical attachment level, increase in Width of Keratinized Gingiva. Therefore the placental allograft is a viable alternative option for root coverage procedure in cases where there is a lack of autogenous connective tissue available to treat gingival recession defects or the patient is unwilling for a second site of surgery. **Principal findings:** The available evidence suggests that Coronally Advanced Flap (CAF) combined with amnion/chorion membranes has significant effect on recession coverage, gain in clinical attachment level, and increase in Width of Keratinized Gingiva. The membrane has also shown to be effective on the gingival biotype, changing to a thick biotype. **Practical implications:** The placental allograft is a viable alternative option for root coverage procedure in cases where there is a lack of autogenous connective tissue available to treat gingival recession defects or the patient is unwilling for a second site of surgery.

**Keywords:** Amnion chorion membrane, Coronally advanced flap (CAF) guided tissue regeneration (GTR) Periodontal Regeneration, root coverage.

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## INTRODUCTION

Gingival recession is defined as the apical migration of the gingival margin beyond the CEJ [1]. As a consequence, the damage to soft tissues leads to exposed root along with loss of attachment and bone loss.

According to Wennström J. L the term “marginal tissue recession” is considered to be more accurate than “gingival recession,” since the marginal tissue may have been alveolar mucosa [2]. The prevalence of gingival recession is common, it may be localized or generalized and can be associated with one or more tooth surfaces [3]. The etiology of the condition is multifactorial including excessive and improper toothbrushing, destructive periodontal disease, fenestration and dehiscence of the alveolar bone, abnormal tooth position in the arch, aberrant path of eruption of the tooth and individual tooth shape, high

muscle attachment, aberrant frenal pull, occlusal trauma, iatrogenic factors (such as orthodontic, or prosthetic treatment) and smoking [4].

The result of recession often is not esthetic and may lead to sensitivity and root caries also making the exposed root surface prone to abrasion.

Management of recession and its sequelae is based on a thorough assessment of the etiological factors and the degree of involvement of the tissues. Esthetics is the primary indication for root coverage surgical procedures.

The international literature has thoroughly documented that gingival recession can be successfully treated by several surgical approaches, their modifications and combination with autogenous soft tissue grafts [5]. Subepithelial connective tissue graft has been considered as the ‘gold standard’ procedure in

the treatment of recession-type defects mainly Millers Class I and II, as it provides a significant root coverage, clinical attachment and keratinized tissue gain [6].

CAF with its modifications is the first choice in patients with high esthetic expectations, when there is adequate keratinized tissue apical to the root exposure. With this approach, the soft tissue used to cover the root exposure is similar in color, texture and thickness to that originally present at the buccal aspect of the tooth with recession defect.

Another concept of recession coverage revolves around Guided tissue regeneration based on Melcher's concept on compartmentalization (1976) experimentally and histologically verified by studies by various authors, which suggests that under physiological conditions, only cells from PDL can synthesize and secrete cementum to attach newly synthesised collagen fibres to tooth [7]. GTR includes procedures by which a barrier is utilized to exclude epithelium from root surface [1]. Recently placental derived membranes have gained importance and have been advocated in the treatment of gingival recession. Placental tissues harbour stem/progenitor cells with properties which make them attractive candidates for application in regenerative and reparative procedures. Moreover, considering that the placenta is normally discarded after birth as medical waste, its procurement as a cell source is easy and raises no ethical controversy [8]. The amniotic membrane is a tissue of fetal origin and is composed of three major layers: A single epithelial layer, a thick basement membrane and an avascular mesenchyme [9]. It contains no nerves, muscles or lymphatics and can be easily separated from the underlying chorion. The fetal membrane was first used for the transplantation of skin in 1910 [10].

Owing to its properties the use of this novel membrane has been advocated in periodontal surgeries. The membrane contains a variety of specialized proteins such as fibronectin, laminin, proteoglycans, glycosaminoglycans and collagen type IV, V and VII. It not only provides a matrix for cellular migration and proliferation but also enhances the wound healing process [12]. It contains a large number of cytokines including transforming growth factor- $\beta/\alpha$ , vascular endothelial growth factor, epidermal growth factor, platelet-derived growth factor- $\beta/\alpha$  and fibroblast growth factor.

It has been reported to be nonimmunogenic, to reduce inflammation, reduces scar tissue, has antibacterial properties, reduces pain at the site of application and acts as a natural biological barrier. Such wound modulating properties make it an interesting new option for application in oral wound healing [13].

Velez and co-workers analyzed the effects of cryopreserved amniotic membrane (CAM) on periodontal soft tissue healing and observed that it was effective in helping cicatrization, wound healing, epithelization, facilitated migration and reinforced adhesion [14].

The results from various reports are encouraging and demonstrate that the amnion allograft is well tolerated by the gingival tissues and results in excellent healing.

Hence a systematic review determining the efficacy of placental derived membranes in patients with class I and Class II Millers isolated/multiple recession with or without comparing it to CAF is undertaken in this study.

Systematic reviews have gained an important position in the dental literature, aiding in clinical decision making. The value of a good systematic review is that it minimizes bias, provides a comprehensive and overview and is objective in its appraisal of quality [15]. So far, no systematic review on the efficacy of Placental derived membranes in treating Millers Class I and Class II recession has been performed. Therefore, the aim of this study was to gather and evaluate, in a systematic manner, available data on the efficacy of Placental derived membranes (Amnion/Chorion) in treatment of Millers Class I and Class II recession defects.

## MATERIALS AND METHODS

### Eligibility Criteria

1. Case reports/ case series using amnion/chorion membrane in treatment of gingival recession.
2. Presence of atleast one experimental group in which amnion/chorion was used for the treatment of gingival recession.
3. Report of gingival recession coverage percentage at baseline and at the follow up period.
4. Case series/case reports with a minimum follow-up of 6 months.
5. Articles published between 2000-2018 were included.

Participants: patients with Millers Class I/ Class II gingival recession above the age of 20 years.

Intervention: treatment with CAF+ Amnion and/or treatment with CAF+Chorion membrane.

Comparison: coronally advanced flap alone.

Outcome measures: to be assessed in terms of gain in clinical attachment level and root coverage percentage.

Study design: case reports/ case series with a follow up of at least 18 months.

### Exclusion Criteria

1. Articles that have a follow up period of less than 6 months.
2. Periodontal infrabony defects extending apically.
3. Literature reviews, randomized control trials were excluded.
4. Unpublished and grey literature.

### Information Sources

For the identification of case reports/ case series to be considered for the inclusion in this systematic review, Pubmed, MEDLINE, Google Scholar, Google and Ebscohost were employed as electronic databases and a literature search was searched for human studies published until December 2018. A specific search strategy was developed for MEDLINE (Appendix) and revised for the other databases. All articles published only in English language were selected. All reference lists of the selected studies were checked for cross references. A hand search of the most relevant journals between 2000 and 2018 was also performed in the college library. Search for gray literature was not attempted.

### Study Selection

The primary search was done by independently screening the titles and abstracts. Further evaluation was done by reading full manuscript of those studies meeting the inclusion criteria or those with insufficient data in the title and abstract to make a clear decision. The articles showing incompleteness regarding the clinical data required as per the aim of the study were eliminated (Figure-1). Screening was done independently and confirmed by the post-graduate guide.

### Summary Measures

**The result measurements were considered as follows:**

#### Main outcome

1. Root coverage

#### Secondary outcomes

1. Width of keratinized gingiva
2. CAL gain
3. Gingival biotype

## RESULTS

After full texts selection 8 articles were included (Figure-1). Characteristics of included studies are presented in Table-1.

All the 8 studies showed a significant increase in root coverage. Mean root coverage is shown in (Table-2). The mean percentage recorded in 4 out of 8 studies of groups with amnion/chorion membranes was higher than their comparators ranging from 22% to 100% (Table-3). The WKG was recorded in 7 out of 8 studies and a significant increase was seen in all studies (Table-4). CAL was recorded by 4 authors (Table-5).

The study by Chakraborty S *et al.*, [16] mean decrease in length of recession (LR) for Chorion site was  $2.00 \pm 1.54$  mm and amnion site was  $1.58 \pm 1.14$  mm. The gain in attachment level for amnion site was  $2.17 \pm 1.53$  mm and for chorion site was  $1.58 \pm 1.22$  mm. The total mean percentage of root coverage was 34% for chorion site and 22% for amnion site.

The study by Pundir *et al.*, [17] followed a split mouth design with 2 groups. Modified CAF with Amniotic Membrane (group A) and Chorion (group B). The gain in recession height for group A was  $1.04 \pm 0.36$  and group B was  $1.30 \pm 0.46$ . The mean CAL at 6 months postoperatively was  $1.04 \pm 0.64$  for group A and  $1.01 \pm 0.80$  for group B. The gain in CAL from the baseline to 6 months postoperatively was 83.85% for group A and 77.93% for group B. Statistically significant difference was found in WKG from baseline to 3 and 6 months in both groups. At 6 months the mean WKG was  $4.334 \pm 0.144$ , for group B  $4.535 \pm 0.174$ . The mean difference in WKG values between group A and B at 6 months was 0.11 and 0.2 respectively.

In the study by George SG *et al.*, [18] patients were divided into two groups. Group I (control) CAF alone using Zucchelli's technique. Group II (test) CAF along with placental membrane. Group II showed a statistically significant mean CAL gain compared to group I from baseline to day 90 ( $P = .007$ ) and from baseline to day 180 ( $P = .006$ ). For mean changes in HGR, group II showed a greater reduction than group I from baseline to day 90 ( $P = .012$ ) and from baseline to day 180 ( $P = .004$ ). Group II also showed a statistically-significant increase in WKT compared to group I from baseline to day 90 ( $P = .007$ ) and from baseline to day 180 ( $P = .006$ ). 2 articles out of 8 checked for the efficacy of placental membranes when combined with CAF.

In the study by Nevins M *et al.*, [19] the mean RW change from baseline to week 24 was statistically significant, decreasing from  $4.05 \pm 1.04$  mm to  $3.00 \pm 1.65$  mm (mean improvement of  $1.05 \pm 1.23$ ;  $P < .001$ ). The mean root coverage at week 24 was 56%. A statistically significant difference in mean CAL between baseline ( $6.12 \pm 1.75$  mm) and week 24 ( $3.46 \pm 1.28$  mm), with a mean improvement of  $2.65 \pm 1.57$  mm, was noted ( $P < .001$ ). A statistically significant difference was also noted for KTW change ( $0.86 \pm 1.21$  mm,  $P < .001$ ). The root coverage success rate on anterior teeth versus posterior teeth and maxillary versus mandibular teeth was compared. A statistically significant reduction in RW in the anterior teeth ( $P = .01$ ) and gain in CAL in the mandibular arch ( $P = .003$ ) were found. The percentage of root coverage for mandibular teeth was 65%, while for maxillary teeth it was 53%. The percentage of root coverage

for the posterior teeth was 50%, while for the anterior teeth it was 61%.

In a study by Esteves J *et al.*, [20] the results showed statistically significant improvements in all clinical parameters. 14 of the 21 GR defects showed 100% GR coverage. The mean change in CAL from baseline to 6 months was  $3.48 \pm 1.21$ . The mean change in GRH at 6 months was  $2.76 \pm 1.00$ . The mean WKG at 6 months was  $1.33 \pm 1.32$ . Change in gingival biotype was evaluated at 6 months, 9 of 21 GRs at baseline with thin biotype had developed a thick biotype.

In a study by Mahajan R *et al.*, [21] comparative evaluation was done between CAF+placental membrane (amnion) (Group I) and CAF+collagen membrane (Healiguide™) (Group II) Significant improvements were observed in both groups. However, intergroup comparison of these parameters yielded nonsignificant differences. A

significant increase in gingival thickness was observed in Group II in comparison to Group I.

The study by Rehan M *et al.*, [22] compared CAF +AM (Group I), CAF+PRF (Group II). The results showed statistically nonsignificant ( $P < 0.01$ ) difference in all clinical parameters at the 6- and 18-month follow-ups in both groups. The authors also recorded the change in gingival thickness, for group I the value was  $0.20 \pm 0.42$  (0.168) for Group II  $0.20 \pm 0.42$  (0.168). Inter-group comparison showed a difference of  $0.00 \pm 0.55$  (1.000).

Jain A *et al.*, [23] in their study compared CAF+ PRF (Group-A) CAF+ Amnion (Group-B) The value for width of Keratinized gingiva (mm) recorded at 6 months for Group A was  $3.267 \pm 0.594$  for group B the value was  $3.667 \pm 0.488$ . Mean difference in the two Groups for WKG showed a significant increase in Group B ( $p < 0.02$ ) as compared to Group A ( $p < 0.04$ ).

**Table-1: Study Characteristics**

Study ID	Author	Location and Year	Follow Up Period	No of Patients	No of Sites	Condition	Group 1	Group 2	Evaluation
1	Chakraborty S <i>et al.</i> ,	Bangalore India 2015	6 months	24	-	Miller's class I and II gingival recession	Amnion+ CAF	Chorion + CAF	gingival recession coverage
2	Pundir A. J <i>et al.</i> ,	Chhattisgarh India 2015	6 months	6	12	Miller's class I gingival recession	Amnion +modified CA	Chorion + modified CAF	gingival recession coverage
3	George, S. G <i>et al.</i> ,	Chennai, India 2018	6 months	15	60	Miller's class I and II gingival recession	CAF	CAF + placental membrane	gingival recession coverage
4	Nevins, M <i>et al.</i> ,	Massachusetts ,USA 2016	6 months	19	43	Miller's class I and II gingival recession	CAF+ Placental membrane (anterior teeth)	CAF + placental membrane (posterior teeth)	gingival recession coverage
5	Esteves, J <i>et al.</i> ,	India 2015	6 months	10	21	Miller's class I gingival recession	Modified CAF+ chorion membrane	-	gingival recession coverage
6	Mahajan R <i>et al.</i> ,	India 2018	6 months	12	-	Miller's class I gingival recession	Amnion+ CAF	CAF + Healiguide™	gingival recession coverage
7	Rehan M <i>et al.</i> ,	India 2018	18 months	16	-	Miller's class I and II gingival recession	Amnion+ CAF	CAF+ PRF	gingival recession coverage
8	Jain A <i>et al.</i> ,	India 2017	6 months	30	-	Miller's class I and II	CAF + PRF	CAF + amnion	gingival recession coverage

**Table-2: Mean Root Coverage**

Author	Baseline Group-1 Mean±SD	Followup Group-1 Mean±SD	Baseline Group-2 Mean±SD	Followup Group-2 Mean±SD
Chakraborty S <i>et al.</i> ,	7.33±1.44	5.75±1.14	7.00±1.86	5.00±1.54
Pundir A J <i>et al.</i> ,	3.05±0.96	1.04±0.36	3.16±0.86	1.30±0.46
George, S. G <i>et al.</i> ,	2.63 ± 0.765	1.43 ± 0.568	2.87 ± 0.9	1.00 ± 0.00
Nevins, M <i>et al.</i> ,	4.61±1.73	1.65±0.88	4.40±1.05	2.10±0.97
Esteves, J <i>et al.</i> ,	3.14 – 1.24	0.38 – 0.59	--	--
Mahajan, R <i>et al.</i> ,	3.17±0.83	0.83±0.80	3.08±0.79	1.25±0.83
Rehan, M <i>et al.</i> ,	1.80±0.92	1.90±1.88	1.50±1.53	1.50±1.53
Jain, A <i>et al.</i> ,	2.733±0.799	1.400±0.633	2.8±0.862	1.000±1.000

**Table-3: Mean Percentage of Root Coverage**

Author	Group 1	Group 2
Chakraborty S <i>et al.</i> ,	22%	34%
Pundir A. J <i>et al.</i> ,	--	--
George, S. G <i>et al.</i> ,	--	--
Nevins, M <i>et al.</i> ,	61%	50%
Esteves, J <i>et al.</i> ,	89.92% – 15.59%	---
Mahajan, R <i>et al.</i> ,	73.31%	59.03%
Rehan, M <i>et al.</i> ,	--	--
Jain, A <i>et al.</i> ,	--	--

4 out of the 8 studies have recorded the mean percentage of root coverage as follows:

**Table-4: Width of Keratinized Gingiva'**

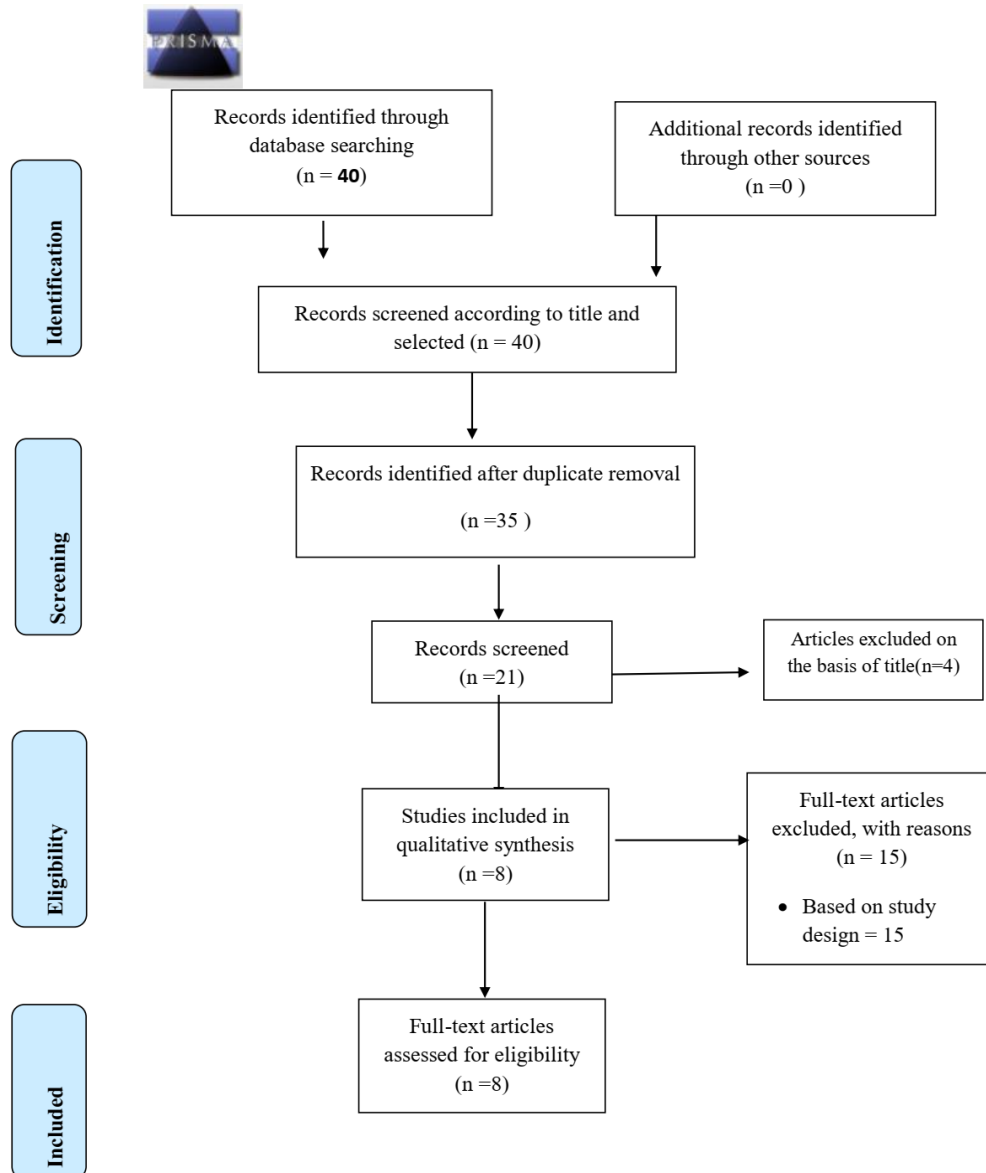
Author	Baseline group 1	Followup group 1	Baseline group 2	Followup group 2
Chakraborty S <i>et al.</i> ,	3.42±0.51	4.42±0.51	3.33±0.49	4.75±0.45
Pundir A J <i>et al.</i> ,	3.309 ± 0.105	4.334. ±0.144	3.465 ± 0.133	4.535 ±0.174
George, S.G <i>et al.</i> ,	1.73 ± 0.785	2.43 ± 0.971	1.50 ± 0.731	3.80 ± 0.551
Nevins, M <i>et al.</i> ,	1.65±1.11	2.57±0.90	1.50±1.15	2.30±1.13
Esteves, J <i>et al.</i> ,	3.00 – 1.00	4.33 – 1.53	--	--
Mahajan, R <i>et al.</i> ,	--	--	--	--
Rehan, M <i>et al.</i> ,	1.10±1.10 (0.012)	0.90±1.37 (0.068)	0.80±1.03 (0.037)	0.80±1.03 (0.037)
Jain, A <i>et al.</i> ,	2.733 ±0.704	3.267 ±0.594	3.000 ±0.535	3.667 ±0.488

**Table-5: Gain in Clinical Attachment**

Author	Group 1 Baseline	Group 1 Follow up	Group 2 Baseline	Group 2 Follow up
Pundir A. J <i>et al.</i> ,	4.13 ± 0.85	1.04 ± 0.64 83 .85%	4.03 ± 0.74	1.01 ± 0.80 77.93%
George, S. G <i>et al.</i> ,	4.50 ± 1.408	2.83 ± 0.791	4.93 ± 1.143	2.20 ± 0.407
Nevins, M <i>et al.</i> ,	6.13±2.12	3.48±1.38	6.10±1.25	3.45±1.19
Esteves, J <i>et al.</i> ,	4.67 – 1.39	1.19 – 0.87	--	--
Mahajan, R <i>et al.</i> ,	4.16±0.83	1.70±0.86	4.12±0.80	1.90±0.94
Rehan, M <i>et al.</i> ,	1.50±1.35	1.60±1.26	1.00±1.05	0.90±1.20

6 out of the 8 studies have recorded the gain in CAL as given in the table respectively.





**Figure-1: PRISMA 2009 Flow Diagram**

## DISCUSSION

Gingival recession has been associated with dentinal hypersensitivity, root caries and esthetic Compromise. A number of grafts have been used in different clinical trials with different degree of success. Literature indicates that the subepithelial connective tissue graft is the most predictable root coverage surgical procedure, considered as a ‘gold standard’ technique, in which a bilaminar vascular environment is created to nourish the graft. However, harvesting the graft from the palatal area increases post-operative morbidity, is time consuming and only a limited amount of donor tissue is available which is insufficient for coverage of multiple recession defects.

Coronally Advanced Flap procedure (CAF) has been tried with varying degrees of success to cover the recession defects. Histologically, this technique leads to reformation of junctional epithelium and the

connective tissue attachment with minimal bone repair but is not stable over long period. Thus, there has been a desire to find a substitute for the autogenous donor tissue.

Placental allografts are now emerging as a novel and material in periodontal plastic surgery. The foetal membranes possess unique inherent biologic properties that enhance wound healing and may propagate periodontal regeneration. In this systematic review, 8 studies were included. 2 out of the 8 studies compared CAF+amnion with CAF +chorion. The authors have concluded that providing a rich source of stem cells, enhancement of healing and self-adhering property make these membranes an effective option for root coverage procedures [16, 17].

2 studies compared CAF+ placental membranes to CAF+ PRF. The studies demonstrated

that both CAF + PRF and CAF + AM are equally effective in providing clinically significant outcomes with respect to root coverage with AM showing better percentage of root coverage as compared to PR [21, 22]. The membrane has also shown to be effective on the gingival biotype, changing to a thick biotype in a duration of 6 months [20].

## LIMITATIONS

1. All the studies have different test and control groups.
2. The same regions have not been selected. This may act as a limitation as the process of healing is known to be different in different areas of the oral cavity.

## FUTURE IMPLICATIONS

The placental allograft is a viable alternative option for root coverage procedure in cases where there is a lack of autogenous connective tissue available to treat gingival recession defects or the patient is unwilling for a second site of surgery. The membrane is an immune privileged tissue possessing antibacterial properties, rich source of stem cells, growth factors, providing enhancement of healing and has self-adhering property and provide a protein-enriched matrix to facilitate cell migration fulfilling the principle of GTR and a novel membrane. It makes site preservation less technically demanding, allows for rapid wound closure, excellent early healing, and provides consistent results. Of all the benefits offered, the ability to be left exposed to the oral environment separates it from traditional collagen membranes, which rapidly degrade in the presence of salivary enzymes. All the properties of the placental membrane make it an excellent option for the treatment of not only recession coverage procedures but also in regenerative periodontal and implant surgery. Therefore, more studies must be conducted for a longer duration of time to support the efficacy of this novel membrane.

## CONCLUSION

Based on the results obtained from the present systematic review, it can be concluded that placental derived membranes are effective in gingival recession coverage when compared to CAF alone or CAF with PRF. The results indicated that, placental membranes showed a better reduction in probing pocket depth, gain in clinical attachment level and better recession coverage.

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