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Investigating the Causes and Effects of Alveolar Bone Loss and the Impact of Restoration Types; A Systematic Review Analysis

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ABSTRACT

Alveolar bone loss has now been identified as a growing problem among various periodontal diseases. Several restoration methods are being adopted depending upon the type of periodontal diseases. The present study aimed to investigate different causes and effects of alveolar bone loss along with the impact of restoration types on alveolar bone loss. A systematic review approach is followed to propose results for the intended objectives. A total of 14 studies were selected based on the inclusion and exclusion criteria for systematic review analysis that falls in the duration between Jan 2000 to Jan 2019. Ovid database, EMBASE, and Web of Science were used to search the given studies. Keywords such as; prostheses or restoration, loss of alveolar bone and types of restoration, orthodontic tooth movement or alveolar ridge preservation were selected. The articles providing information about the preservation of alveolar bone in clinical context, periodontal health conditions, and bone density around implants were included in the review; whereas, the articles with abstracts only and the remodeling process of implants were excluded. The risk of biasness was analyzed through Cochrane Collaboration's tool. Reasons such as overhang fillings, impact of statins, subgingival calculus, oxidative stress, etc. were identified. Besides, the given studies are significant in indicating the effectiveness of different restoration types. The study concluded that there is a need to provide clinical trials regarding the impact of restoration types and causes of alveolar bone loss.

Key words: *Alveolar Bone Loss, Restoration Types, Periodontal Diseases.*

INTRODUCTION

Defects in alveolar bones are mainly restored through different methods that help in managing the sustainability of alveolar bones. Patients undergoing through problems in alveolar bone are usually treated through orthodontic tooth movements, which according to Lee et al. [1] is one of the most successful methods of bone restoration. Tamimi et al. [2] suggested three important restoration types that can be successfully used for treating problems of alveolar bone, such as alveolar ridge. The types include bone augmentation [3], guided bone regeneration [4, 5], and distraction osteogenesis [6]. In certain cases, periodontitis or trauma results in the reduction of bone volume as a result of tooth loss. [3]

AlJehani [7] demonstrated that the prevalence of bone loss is more frequent among individuals aged above 70, provided that the mean rate of bone loss is up to 0.288 mm in comparison to the annual rate of bone loss. The occurrence of alveolar bone loss is due to the increasing time of bacterial plaque that is in continuous contact of periodontal tissues. After extracting tooth, an average of 1.5mm – 2mm vertical and 40 – 50% horizontal alveolar bone loss occur within the time period of 6 months. [8] Moimaz et al. [9] indicated another significant cause of alveolar bone loss, according to which the problem is mostly found in long term and habitual smokers. Since smoking causes different bacteria in the oral cavity, this leads towards the excessive bone loss along with the formation of periodontal pockets. [10, 11] Trauma, periodontal disease, and periapical pathology may lead to loss of the alveolar bone volume.

For various scholars, tooth extraction causes problems related to periodontal tissues resulting in alveolar bone loss. Barone et al. [12] suggested some other causes of bone loss that includes trauma, congenital alveolar defects, atrophy, periodontal diseases and tumor resection.

Mostly changes in the alveolar dimensions take place in the first 3 months after restoration. The bone loss leads to 40 – 60% loss of ridge volume during the first three years if no treatment is provided for restoring the dentition. [3] With respect to the success of implant and its survival, lack of sufficient bone height and volume is considered detrimental to the final treatment outcome. The success of esthetic or functional restoration used in rehabilitation of partially and completely edentulous patients is dependent on its optimal placement. However, its placement is significantly affected due to height, alveolar ridge dimensions, and buccolingual position. [13]

Disruption of the alveolar bone leads to restoration of functional conditions that are integrated through the endosseous implants. [14] There is a negative impact of implant placement on the alveolar ridge after removal of tooth, causing bone resorption and remodeling that is a natural healing process. [13] There is a prominent root position in the anterior region of maxilla that is accompanied by fine and fragile vestibular wall. The vestibular wall is likely to get damaged during tooth extraction. The vestibular walls play an important role in managing the process of alveolar bone restoration. Therefore, restoration of the remaining alveolar ridge is to fulfil the contemporary requirements of prosthetic implant placement. The fixed prosthesis after interproximal amalgam restorations is a major cause of periodontal disease. However, wrong placement of margins during amalgam restoration may create an adverse effect on the alveolar bone. [15]

There is a direct association between type of restoration and its placement, and prevalence of periodontal disease. The development of periodontal disease is also associated with materials used for implant restoration. Majority of the restorative materials are biocompatible and do not have a negative impact on the periodontal tissues, except for the self-curing acrylics. [15] The accumulation of plaque is prevented through a highly polished surface inhibiting the initiation of periodontal disease. Chen et al. [16] determined the influence of the abutment height over peri-implant marginal bone loss. The study elaborated that the success of tooth implant is mainly based on marginal bone loss. Initial bone loss within the process is largely dependent on psychological factors. The findings of the study indicated no significant association between early marginal bone loss and cofounding factors. Dal Piva et al. [17] conducted a study to determine the influence of the alveolar bone loss along with thickness of layer on the biochemical behavior of endodontically treated maxillary incisors. A finite element analysis was conducted. Examinations were made under two different thickness and lengths of bone loss. The findings of the study indicated that more cement concentration, dentin and fiberglass posts were associated to the bones with increased alveolar bone loss. Moreover, maximum thickness of cement layer is associated with more stress on the alveolar bone.

Studies have shown that various surgical materials and techniques are used for successful placement of the dental implants within the resorbed alveolar bone. It is believed that the denture foundation and patient satisfaction is improved due to the presence of implant beneath partial or complete denture. The information regarding the influence of restoration methods on the loss of alveolar bone. Therefore, the present study aims to investigate the impact of restoration methods and their influence on alveolar bone loss. It further outlines different causes of alveolar bone loss.

METHODOLOGY:

A systematic review of literature was conducted to investigate the impact of restoration and their influence on alveolar bone loss, along with different causes of the alveolar bone loss. The overall methodological practices involved in this study are held through the researcher's compliance to Preferred Reporting Items for Systematic

Reviews and Meta-analysis (PRISMA). Since only few studies provided similar outcomes, the study failed to perform meta-analysis.

Procedure

Studies from Jan 2000 to Jan 2019 were included for the systematic review. Ovid databases, EMBASE and Web of Science were used for searching relevant studies. Furthermore, bibliography of publications that fall within the same time duration and below provided inclusion and exclusion criteria was studied to expand the sources of researching. The keywords used for searching databases included loss of alveolar bone and types of restorations, prostheses or restoration, orthodontic tooth movement or alveolar ridge preservation. The filters of English article and dental journals based on human studies were applied in all databases.

Identifying and Collecting Articles

The inclusion criteria for different publications was based on study designs. However, randomized controlled trials, cohort studies, case control studies, experimental studies, case reports along with full text articles written in English language were included in the inclusion criteria. The articles reporting about preservation of alveolar bone in clinical contexts were included in the study analysis, which helped us identify the causes of alveolar bone loss and the techniques of preservation. [18] There was extensive involvement of the studies that were related to the improved bone density around the implants, periodontal health conditions and systemic diseases. Studies in relation to the given issues are important as they cause bone loss. In contrast to this, the articles with only abstracts and remodeling process of implant body were excluded, as the prime focus is to provide the causes of alveolar bone loss along with the impact created by different restoration techniques. Moreover, the articles concerning problems other than alveolar bone were excluded from the searched criteria. Figure 1 illustrates the procedure of data collection through review of different related studies.

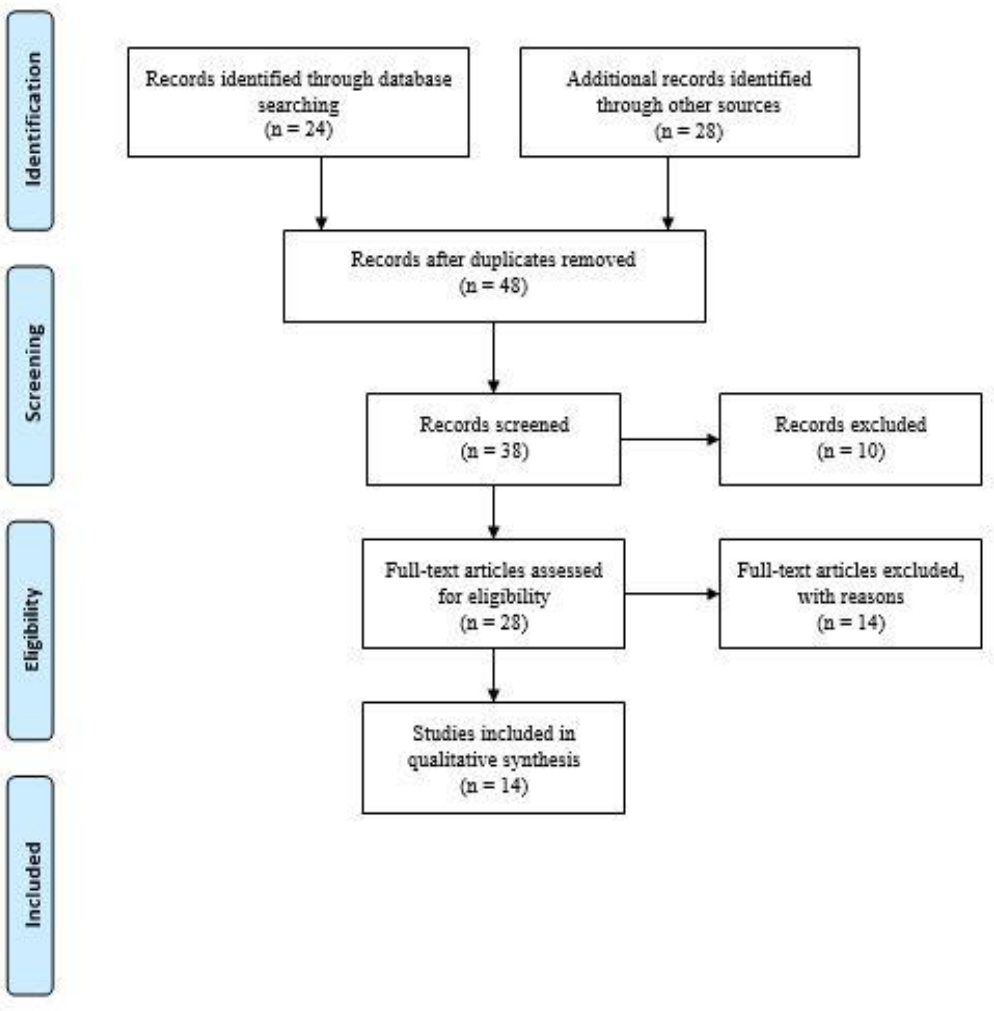

Figure 1: PRISMA Flow Diagram

Data Extraction

Data were independently extracted by the contribution of two reviewers, in case of an ambiguity, a third reviewer assisted the study. The studies that were totally complied on the inclusion criteria were included, and those that consisted sufficient information in their abstracts were involved in the full text assessment carried by the reviewer to identify and determine the eligibility of the study. The selected studies further underwent the process of validity assessment along with extraction of data. The reasons that were considered for the rejection of different studies were also recorded. The extraction and recording of data were based on the following variables; a) study type b) participants' characteristics, c) duration of participants follow-up d) intervention characteristics e) sample size f) source of funding and conflicts of interest, methods of randomization.

Risk of Bias and Qualitative Analysis

The study was designed and reviewed by two reviewers to ensure that the study is in accordance to PRISMA guidelines to avoid risk of biasness while providing the quality evidences. Besides, the evaluation of the included articles was also undertaken to maintain the originality of this review. The methodological quality of the observational studies that were included, were assessed through the Newcastle Ottawa Scale (NOS). The study guidelines provided by the National Institute of Health Research PROS-PRES were also followed. Risk of biasness of the studies were tested using Cochrane Collaboration's Tool as indicated in Figure 2.

Different techniques associated with the restoration methods of loss of alveolar bone were studied in the selected studies. The primary outcome of the analyses provided that overhang, implant restorations loading, and restoration timings are some considerable factors that are associated to the alveolar bone loss.

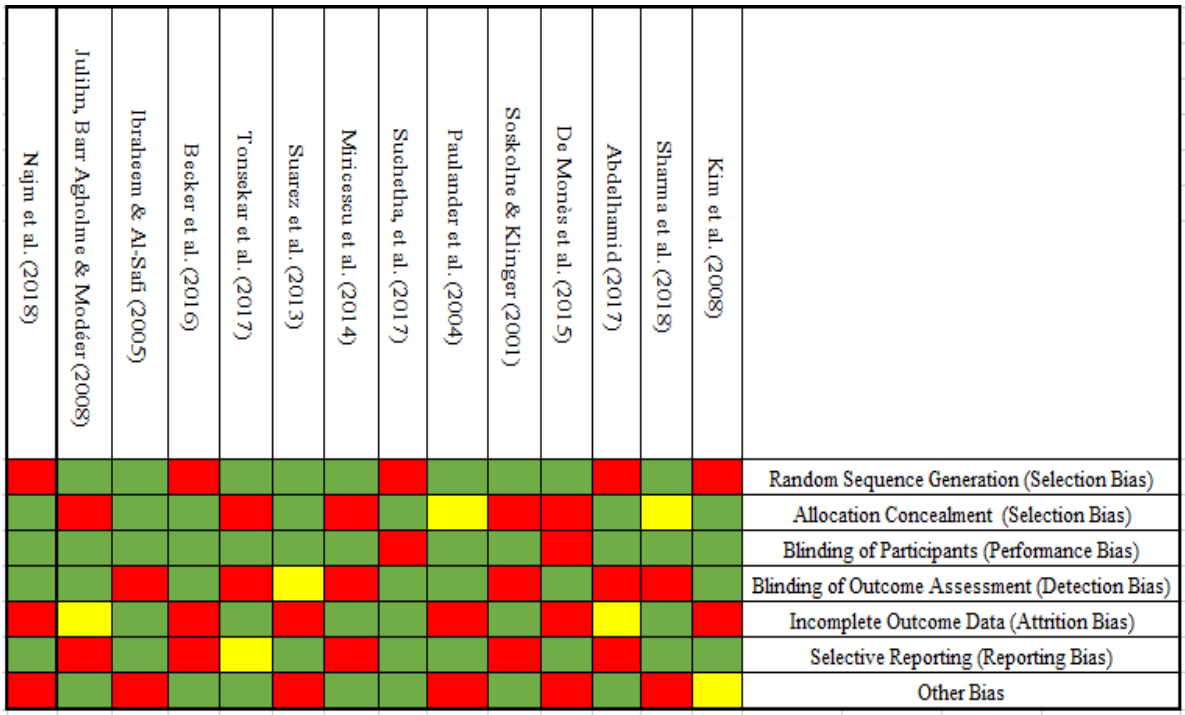

Figure 2: Risk of Biasness

RESULTS:

To identify different causes of alveolar bone loss along with the impact of treatment methods for alveolar bone restorations, 14 studies were selected based on the inclusion criteria of the study. Among these, 5 were original articles, 4 were review articles and remaining 5 included, case studies, cohort study, prospective study, narrative review and longitudinal study.

Najm et al. [19] assessed the relationship between overhang filling and alveolar bone loss. Total of 900 digital panoramic radiographs were examined to identify the presence of overhang amalgam. Among the selected images, only 80 were found with overhang fillings. The overhang filling surface of the alveolar bone loss was compared with normal surface of similar tooth. The results indicated through radiographical images suggested that the overhang amalgam was found mostly in mandibles in firsts molars. Besides, the overhang filling in alveolar bone

loss has significantly increased the overhang filling unto 3.73mm and 4.31mm; while, the normal surface is up to 1.4mm-1.9mm respectively. Also, mandibular teeth were found significant in undergoing through bone loss, when compared to maxilla.

Julihn, Barr Agholme and Modéer [20] conducted a study regarding the incipient of alveolar bone loss. The study follows a cross-sectional design where 800 people were randomly selected. The results of the study indicated that the participants with subgingival calculus, proximal restorations were at higher risks of alveolar bone loss. Ibraheem and Al-Safi [21] conducted a study to identify the formation of overhang margins while providing the important effect on periodontal status. To identify the prevalence, a sample consisting of 100 patients was used in this regard. The findings of the study indicated that overhang margins are significant in creating a direct impact over alveolar bone loss. Besides, a significant difference was detected between tooth restored with overhang and without overhang. Miricescu et al. [22] conducted a study to identify the relationship between salivary biomarkers of oxidative stress and alveolar bone loss. The study included 20 patients experiencing severe periodontal disease. The findings of the study indicated that the patients undergoing through periodontal diseases supported oxidative stress that was related to the alveolar bone loss. It further identified that oxidative stress was high among the patients with periodontal diseases.

Abdelhamid [23] proposed important knowledge regarding the preservation of alveolar bone from significant loss. The information provided in the study regarded a significant emphasis towards the preservation of periodontal soft tissues and bone volume during tooth extractions. The study further provided that the preservation of alveolar socket is important to assure the preservation of alveolar bone. In contrast to this, poor treatment methods for tooth extraction may lead to the occurrence of alveolar bone loss.

Next include studies conducted through systematic reviews. Tonsekar et al. [24] identified the relationship between periodontal diseases and dementia through systematic reviews of researches before 2016 searched through electronic databases. However, out of 756 articles, only 16 articles were analyzed. The findings of the study illustrated that from the total articles, four studies provided positive association between dementia and multiple tooth loss. Another study evaluated that chronic periodontal disease such as the alveolar bone loss was significantly associated to dementia. Other 8 studies identified that cognitive impairment shares a significant relationship with bone loss. Suarez et al. [25] conducted a systematic review to identify the impact of restoration timings on the implant marginal bone level. The review aimed to identify the impact of marginal bone loss that was successfully restored by complying with different conditions that include immediate restoration loading (IRL), conventional and early loading (CL) and (EL). From 1640 articles, only 11 were selected. Meta-analysis of the given studies provided the maximum confidence interval, i.e. 95% for IRL and delayed prosthesis. The results indicated that immediate restoration loading is useful for marginal bone loss.

Suchetha et al. [26] conducted a study to analyze various causes of alveolar bone loss. The study provided that periodontal diseases caused in alveolar tissues are highly associated with the alveolar bone loss. Similarly, alveolar bone defects such as osseous craters, hemiseptal defects, infrabony defects are some major causes of alveolar bone loss. Lastly, furcation involvements measuring up to Grade I and III are identified as some of the main causes of alveolar bone loss. Soskolne and Klinger [27] proposed a cross-sectional study to identify the impact of diabetes on alveolar bone loss. The sample of the study included patients with type I and II diabetes. The results of the study indicated that people with controlled diabetes are exposed to minimum risks of alveolar bone loss; whereas, individuals with poorly controlled diabetes experienced greater alveolar bone loss. Besides, the prevalence of periodontal diseases was also common among such individuals.

Sharma et al. [28] proposed multiple techniques to reduce the amount of bone loss by maintaining the structure of jaw bone crest. However, the results of the study indicated that bone grafting by inducing Le Fort I osteotomy inlay is useful in improving the architecture of jaw bone crest. The study further favors the use of the given approach since the results were in favor to the proposed method and thus helped in managing the alveolar bone loss. Paulander et al. [29] conducted a cohort study of 10 years to identify the risks factors associated with the periodontal bone loss. Data in the given study was collected through an epidemiological survey conducted in 1998. To analyze the prevalence of alveolar bone loss, the level of alveolar bone was measured to identify the longitudinal change. The results of the study indicated that periodontal bone loss occurred up to 0.4mm from 0.22mm. Also, a significant change in terms of increased diseases was detected among smokers in contrast to nonsmokers.

Becker et al. [30] evaluated the status of periodontal health among patients that had undergone through implant treatments. The patients received dental implants since 1995 were included in the study. Demographic details,

quality and quantity of bones, implant location along with the type of study were recorded in the database. The patients aged between 66-93 years were included. NIH (National Institute of Health) images were used to measure the changes in bone levels. The results of the study concluded that the patients with the given provided outstanding survival rates of dental implants, with limited changes in the interproximal bone levels. The treatment was significant in maintaining patient's oral health. De Monès et al. [31] conducted an important study to provide the causes of alveolar bone loss. The aim of the study however, was to provide the impact of statins in minimizing the resorption in alveolar bones. A systematic search was performed through databases such as MEDline and Pubmed, resulting into the selection of 21 studies. The results of the study indicated that the use of statins was highly significant in reducing the oral cavity and the prevalence of periodontal diseases after tooth extraction. Therefore, statins were highly useful in controlling the alveolar bone loss.

Another study undertaken by Kim et al. [32] examined the relationship between alveolar bone loss and root proximity. The study followed a longitudinal cohort design by including a sample of 1231 individuals. Results were proposed by measuring the interradicular distances and alveolar base levels through digitalized radiographs. The findings of the study indicated a significant nonlinear relationship between alveolar bone levels and interradicular distance.

Table 1: The Characteristics of the Included Studies

Name of Author	Year of Publication	Title	Type of Study
Najm et al.	[19]	Clinical and Radiographical Assessment of Alveolar Bone Loss Associated with Overhang Amalgam Filling	Original Article
Julihn, Barr Agholme & Modéer	[20]	Risk factors and risk indicators in relation to incipient alveolar bone loss in Swedish 19-year-olds	Original Article
Ibraheem & Al-Safi	[21]	Prevalence of overhang margins in posterior amalgam restorations and alveolar bone resorption	Original Article
Becker et al.	[30]	Dental implants in an aged population: evaluation of periodontal health, bone loss, implant survival, and quality of life.	Prospective study
Tonsekar et al.	[24]	Periodontal disease, tooth loss and dementia: is there a link? A systematic review.	Systematic review
Suarez et al.	[25]	Effect of the Timing of Restoration on Implant Marginal Bone Loss: A Systematic Review	Systematic Review
Miricescu et al.	[22]	Salivary biomarkers: relationship between oxidative stress and alveolar bone loss in chronic periodontitis	Original Article
Suchetha, et al.	[26]	Alveolar bone in disease	Review Article
Paulander et al.	[29]	Some risk factors for periodontal bone loss in 50-year-old individuals: A 10-year cohort study	Cohort study
Soskolne & Klinger	[27]	The relationship between periodontal diseases and diabetes: an overview	Review Article
De Monès et al.	[31]	Statins and alveolar bone resorption: a narrative review of preclinical and clinical studies.	Narrative review
Abdelhamid	[23]	Alveolar Bone Preservation. Biological Basis and Techniques.	Original Article
Sharma et al.	[28]	Multidisciplinary Approach to Correct Alveolar Bone Loss and Vertical Maxillary Deficiency to Restore Dento-Maxillofacial Aesthetics and Functional ability.	Case Study
Kim et al.	[32]	Root proximity as a risk factor for progression of alveolar bone loss: The Veterans Affairs Dental Longitudinal Study.	Longitudinal Study

Table 2: A Detailed Review of Studies

Study	Methods	Results	Significant Outcomes
Najm et al.	Panoramic and radiographic images were used to identify the difference.	The results indicated that the alveolar bone loss increased with overhang	Alveolar bone loss is significant associated with the overhang amalgam fillings.
Julihn, Barr Agholme & Modéer	The study followed a cross sectional design with a sample of 800 participants.	Findings of the study indicated two significant causes of alveolar bone loss in the recruited sample. The causes include; proximal restorations and subgingival calculus.	Patients with subgingival calculus and proximal restorations were more likely towards the risks of alveolar bone loss.
Ibraheem & Al-Safi	Bitewing radiographs were used to detect overhanging margins on different restorations. 1185 restored surfaces provided overhanging margins.	Overhanging dental restorations shares a significant relationship with bone loss.	More alveolar bone loss occurs at surfaces with overhanging restorations, in comparison to those without restorations.
Becker et al.	The study followed a prospective method where patients receiving implant treatment since 1999 were observed.	Findings indicated that patients receiving tooth implant restorations provided significant survival rates of different periodontal issues. Also, minimum changes were recorded in bone levels of patients.	The study identified the need of efficient planning for prosthetic rehabilitations, as it is important for successful tooth implantations.
Tonsekar et al.	The study was conducted through systematic review.	A positives relationship was identified between dementia and periodontal outcomes.	The outcomes of the paper indicated the need for further clinical trials that are related to periodontitis and dementia.
Suarez et al.	Through electronic data search, total of 1640 articles were selected. However, only 11 of them fall into the inclusion criteria of the study.	Results of the study indicated that immediate restoration loading is significant for alveolar bone loss.	Restoration timings have no significant impact on implant marginal bone loss.
Miricescu et al.	The study was conducted by including 20 patients with chronic dental diseases.	Results of the study indicated a positive association between oxidative stress and alveolar bone loss.	The study provided that salivary biomarkers that include oxidative stress is significant in indicating the alveolar bone loss.
Suchetha et al.	The study conducted a review article to provide different causes of alveolar bone loss.	Results of the study demonstrated that periodontal diseases, perpendicular attachment of bone margin and teeth surface, furcation involvement with Grade I and III were some of the major causes of alveolar bone loss.	The structural changes involved in the alveolar bones are important contributors of alveolar bone loss.
Paulander et al.	An epidemiological survey was undertaken conducted in the year 1998 to generate the study sample.	Results indicated smoking as the strongest predictor of alveolar bone loss among participants. It further resulted in increasing the pocket depth and the number of periodontal diseases.	Smoking serves as one of the crucial factors for increasing rate of alveolar bone loss among individuals.
Soskolne & Klinger	A cross sectional design was used in the study.	Participants with uncontrolled diabetes were at major risks of greater alveolar bone loss.	Diabetes serve as one of the major causes of alveolar bone loss among various patients.
De Monès et al.	The study followed a systematic approach by selecting 21 studies in total.	Results indicated that use of statins is important in reducing alveolar bone loss among patients that have undergone through tooth extraction.	Use of statin serve as one of the useful methods in controlling and preventing alveolar bone loss.

Abdelhamid	The study provided a major review of previous studies.	Findings indicated that preservation of periodontal tissue, alveolar socket and bone volume is important during tooth extraction to refrain from alveolar bone loss.	Effective treatment methods may help in preserving alveolar bones through any loss.
Sharma et al.	The study provided information through a case report	Results highlighted that preservation of bone grafting through Le Fort I osteotomy is important to improve the architecture of jaw bone crest, as it helps in reducing the alveolar bone loss.	Managing the structure of alveolar bone crest is important to reduce alveolar bone loss
Kim et al.	The study is conducted through a longitudinal cohort design.	Results proposed a significant nonlinear relationship between alveolar base levels and interradicular distances.	Interradicular distance up to 0.8mm is a significant indicator of alveolar bone loss.

DISCUSSION:

The impact of restoration types and the causes of alveolar bone loss have been identified by providing a systematic review of various researches. Becker and Neronov [33] conducted a case report to analyze the impact of orthodontic elastic separators on loss. The findings of the study indicated that major use of orthodontic elastic separator results in significant alveolar bone loss. Lestari, Azhari and Wendari [34] further reported that the distance between cementoenamel junction (CEJ) and the alveolar bone crest is yet another important cause of alveolar bone loss. [35] Ohnishi et al. [36] provided other important reasons in relation to the alveolar bone loss among various mice. The study aims to evaluate various inducements and their role in initiating alveolar bone loss. Immunohistochemical were used to detect the occurrence of endothelial nitric oxide synthase in mandibles. The findings of the study indicated that among various mice, reactive oxygen related components including hydrogen peroxide is significant in creating loss of alveolar bone. Various diseases such as diabetes that weakens the potential strength of the human body are also important for alveolar bone loss. The results proposed in the study of Preshaw et al. [37] indicated a significant relationship between diabetes and alveolar bone loss. This indicates that alveolar bone losses are also initiated through various health related disease.

Haggerty, Vogel and Fisher [38] in their study mentioned about the methods that help in the long-term sustainability to the dental implant restoration. Special emphases were provided to the implementation of alveolar ridge augmentation that are effective in correcting the alternative mandibular relationships important to correct discrepancies associated to vertical distance found between jaws. This would further help in the addition of the required bone volume for successful implant placement. [39, 40]

Green et al. [41] provided an important stance in this regard. According to the study, assessment of the presence and extent of alveolar bone loss is important to evaluate the changes found in the alveolar bone loss. Sharma et al. [28] provided a case study to introduce the effectiveness of bone grafting with Le Fort I as an effective technique to increase and restore the function and aesthetics of maxillary tooth with severe bone loss. The findings of the study indicated that alveolar bone loss along with functions and aesthetics of alveolar bone loss were effectively restored through the given method, due to significant improvement in face dimensions.

Pejeva et al. [42] conducted a study to determine the influence of dental implants resulting in marginal bone restoration. A special emphasis was granted to the negative effects of alveolar bone restoration when conducted through ossteointegrated dental implants. The findings of the study indicated that the complicated conditions of ossteointegrated dental implant results in the marginal bone resorption leading towards the destruction of the bone tissue.

The systematic review indicated various causes of alveolar bone loss along with the type of restoration methods and their impact. The results proposed in the study are significant and can be implied to patients with periodontal diseases. Several causes are highlighted in this study which are important for clinical experts to make important assessments regarding patients' treatment. Moreover, results can be further implied to patients undergoing through dental problems, as the information provided in the study may help patients to attain timely diagnosis. Dental experts working globally can highly benefit from the study, as it provides an abundant information regarding periodontal diseases that serve as the fundamental cause of alveolar bone loss. This study is sufficient in educating

the target population that includes patients with periodontal diseases and alveolar bone loss along with those intending to undergo restoration treatments, and further serves as a guideline for the effectiveness of different restoration methods.

CONCLUSION:

Different forms of restoration methods have been evolved by the time which creates both positive and negative effects on the strength and placement of the restored tooth. The study is significant in providing valuable outcomes regarding the causes of alveolar bone loss and impact of restoration methods. Information provided in the study is important for professional experts belonging to the given field.

Several reasons have been identified regarding the causes of alveolar bone loss along with the impact of type of restoration treatment. Outcomes such as the overhang amalgamation filling, impact of statins, periodontal diseases, furcation involvement, oxidative stress, overhanging dental restorations, etc. are some important problems that are associated to alveolar bone loss. Other than this, several studies were included to identify the impact of different restoration methods are presented. The results however indicated that certain restoration methods are insignificant in providing maximum survival rate.

The present study is important in shedding light on different types of restoration methods along with their impact. A number of studies are provided in the review to outline some of the major findings that have been developed in the past few years. The findings of the study are useful for clinical expertise, as it provides a variety of knowledge considering the loss of alveolar bone and restoration methods. The results are further critical as they explicitly highlight the pros and cons of different restoration methods along with the causes that ultimately result in the tooth restoration failure. As the study follows a systematic review, it is invalid to propose any accurate results. The study has certain limitations, as only few studies are added in the review. Therefore, a more detailed discussion is required to cover the topic further, through cross-sectional study design.

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