Study on risk factors implicated in post-extraction alveolitis

Riviş M.[1], Todor L.[2], Todor S.A.[3], Cosoraoaba R.M.[4], Popovici R.A.[4], Olariu I.[5], Dinu S.[6]

[1]Department 2, Faculty of Dental Medicine, Victor Babes University of Medicine and Pharmacy, Timisoara, Romania
[2]Department of Dental Medicine, Faculty of Medicine and Pharmacy, University of Oradea, Romania
[3]Dentist doctor, private medical office, Oradea, Romania
[4]Department 1, Faculty of Dental Medicine, Victor Babes University of Medicine and Pharmacy, Timisoara, Romania
[5]Department of Denistry, Faculty of Dentistry, Faculty of Medicine, "Vasile Goldis" Western University of Arad

Correspondence to:
Name: Liana Todor
Address: Department of Dental Medicine, Faculty of Medicine and Pharmacy, University of Oradea, Romania, December 1st Square no.10, 410068 Oradea, Bihor County, Romania
Phone: +40 723517100
E-mail address: liana.todor@gmail.com

Abstract

Post-extraction alveolitis is a complication specific to tooth extraction that can occur during the healing process (usually 24–72 hours after extraction). This complication can occur due to the dislodgement of the blood clot (the first stage of the healing process), following a local infection, poor local hygiene, or factors related to the plasma system. It is estimated that the probability of developing dental alveolitis after an extraction is 3%. In the case of wisdom teeth, the percentage of probability increases to 20% and even 30%.

This paper aims to evaluate one of the complications that can occur after tooth extraction, namely post-extraction alveolitis, as well as on the particularities that can contribute to the development of this complication that leads to the alteration of the patient's general condition and delayed healing.

The retrospective study was carried out on a number of 28 patients hospitalized in Timisoara Oral and Maxillo-Facial Surgery Clinic, who presented post-extraction alveolitis. A series of risk factors are implicated in the evolution of post-extraction alveolitis: surgical trauma, bacterial infections, patient age and sex, oral contraceptives, smoking.

Keywords: post-extraction alveolitis, risk factor, bacterial infection

INTRODUCTION

The links between post-extraction alveolitis and poor oral hygiene, periodontal disease and pericoronitis have led to an extended theory, incorporating a completely extrinsic etiological factor. Certain bacteria show fibrinolytic activity independent of the host response and act directly on the blood clot - Treponema denticola produces its own fibrinolytic enzyme (fibrinolysin) and Prevotella oralis releases proteases that convert plasminogen into plasmin and thus further increase fibrinolysis [1].

The etiopathogenesis of post-extraction alveolitis is not well understood, but it is known that it usually begins around 2-4 days after extraction and is unlikely to occur before the first 24 hours due to the presence of antiplasmin (plasmin inhibitor) which delays fibrinolysis. Only after antiplasmin levels have been reduced does clot lysis occur. Its duration varies between 5 and 10 days [1].

Surgical trauma and the difficulty of the surgical intervention play a significant role in the development of post-extraction alveolitis, this could be due to a greater release of direct tissue activators secondary to bone marrow inflammation following more difficult, therefore more traumatic extractions [2]. Surgical extractions, compared to non-surgical extractions, lead to a 10-fold increase in the incidence of post-extraction alveolitis [2]. In addition, a positive correlation was observed between operator inexperience and increased incidence of post-extraction alveolitis, which could be due to many factors, including prolonged operating time and increased trauma. [1].

Marked or prolonged trauma during an extraction or infection causes increased localized inflammation in the bone that triggers the release of plasminogen activators [1, 2]. They facilitate the conversion of plasminogen to plasmin, which breaks down fibrin and leads to lysis of the blood clot (Figures 1,2) [1, 2]. Plasmin also plays an active role in the production of kinins [1]. Kinins not only propagate the inflammation process by stimulating the release of inflammatory mediators, but have a major role in sensitizing and stimulating pain receptors [1]. All these factors are related to the main characteristics of post-extraction alveolitis, which are clot rupture and severe pain [1].

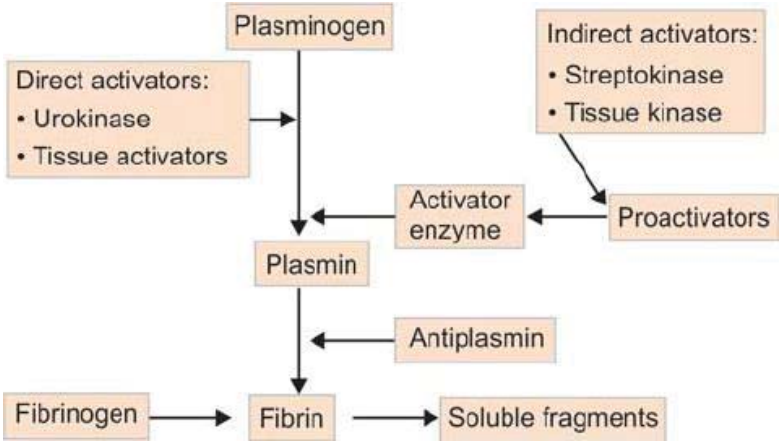

Figure 1. Pathogenesis of post-extraction alveolitis

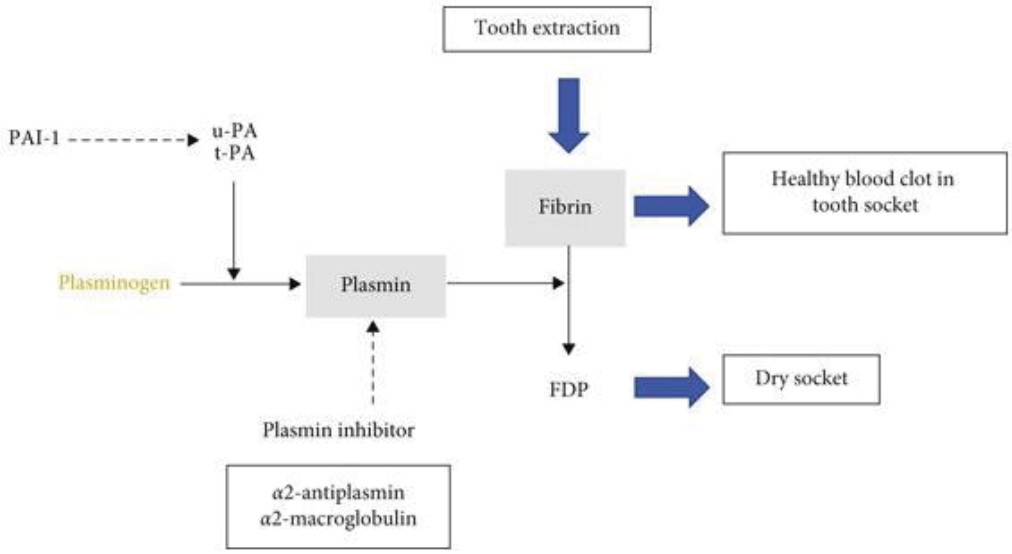

Figure 2. Molecular mechanism of post-extraction osteitis: Plasminogen type-1 is the precursor of plasmin which acts in fibrin degradation. Plasmin inhibitor sterically shields the active site of plasmin, decreasing the access of plasmin to protein substrates. t-PA: tissue-type plasminogen activator; FDP: fibrin degradation products [3]

In the French-speaking literature, a form of wet alveolitis is described that is not found in the international specialized literature [4]. This is characterized by an accumulation of excess granulation tissue at the level of the post-extraction alveolus, moderate pain felt by the patient, the presence of an exuberant, superinfected clot, which can occasionally look like a gingival polyp [4].

Post-extraction alveolitis occurs 2-3 days after extraction. During this period, the blood clot disintegrates, resulting in delayed healing and necrosis of the bony surface of the socket [5]. This disorder is also called fibrinolytic/dry alveolitis and is characterized by an empty cavity, halitosis, bad taste in the mouth, bare bony walls and severe pain radiating to other areas of the head [5].

Aim and objectives

This paper aims to evaluate one of the complications that can occur after tooth extraction, namely post-extraction alveolitis. Another objective is to draw the attention of the dentist and the dentoalveolar surgeon to some aspects and particularities that can contribute to the development of this complication that leads to the alteration of the patient's general condition and delayed healing.

MATERIALS AND METHODS

The first stage of the retrospective study represents the establishment of the clinical characteristics necessary for the selection of patients who presented with post-extraction alveolitis in Timisoara Oral and Maxillo-Facial Surgery Clinic and were included in the study.

Statistics were also made regarding: the total number of patients, the ratio according to sex, the ratio according to age, the distribution of ages according to sex, the ratio of the incidence of dry and wet alveolitis, the number of dental units extracted, the percentage of development of alveolitis at the mandibular and maxillary level, the incidence of associated complications and how many patients presented comorbidities.

The patients were informed about the inclusion in a medical studio and expressed their consent in writing, according to Order of the Ministry of Health 1411 of 12.12.2016,

annex no. 1 to the methodological norms - Form for expression of the consent of the informed patient.

Patient selection and inclusion criteria:

1. Adult patients (over 18 years);
2. Both sexes;
3. The presence of post-extraction alveolitis following the extraction of one or more dental units;
4. Admission to the Oro-Maxillo-Facial Surgery Clinic Timişoara for the possibility of monitoring the patient.

Exclusion criteria:

1. Minor patients (under 18 years);
2. Patients who do not present post-extraction alveolitis;
3. Patients who refused hospitalization;
4. Lack of patient compliance and cooperation;
5. Indiscriminate patients;
6. Patients with acute diseases of the oral mucosa (stomatitis);
7. Patients with acute infectious processes;
8. Patients with malignant tumors cervicofacial located or in the oral cavity;
9. Patients under radio and/or chemotherapy treatment.

The patients were hospitalized in the Timişoara Oral and Maxillo-Facial Surgery Clinic, where they were given anamnesis and clinical evaluation, all data collected to be recorded in the patient file.

Imaging investigations: panoramic radiography or CBCT were requested for imaging evaluation of the case. The role of these paraclinical explorations is to diagnose the presence of alveolar or dental bone fragments at the level of the post-extraction socket, they act as an irritating thorn that prevents or delays the healing of the socket.

During the anamnesis, the patients reported severe, constant pain, with progressively increasing intensity, reaching maximum intensity 2-3 days after the extraction, this being the main reason for presenting to the doctor.

The clinical evaluation highlighted changes in the peri-alveolar oral mucosa, alterations in the healing process located at the level of the post-extraction alveolus, sensitivity to palpation, radiating pain in the neighboring teeth, in the neighboring anatomical areas, pain to touch, irrigation, but no septic process consisting of level of the alveolus or in the surrounding tissues.

RESULTS

The study included 28 patients, 6 men and 22 women, who presented themselves in the Oro-Maxillo-Facial Surgery Clinic Timişoara (Figure 3).

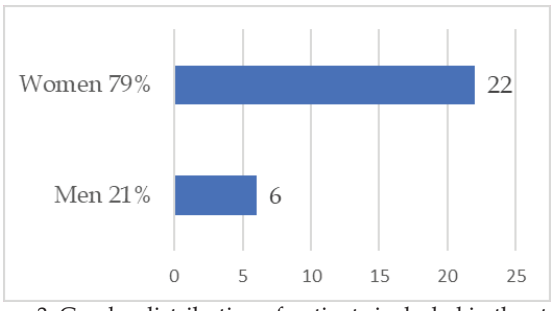

Figure 3. Gender distribution of patients included in the study

Of the 28 patients, 13 (46.43%) were up to 30 years old, 8 patients (28.57%) were between 30 and 49 years old and 7 patients (25%) were over 50 years old (Figure 4).

In the age group <30 years, the number of female patients (9) is higher compared to the number of male patients (4). In the 30-49 age group, patients are only female (8). In the case of the age group ≥50 years, the number of female patients (5) is higher than the number of male patients (2). Therefore, the share of female patients is the majority in all age groups (Figure 5).

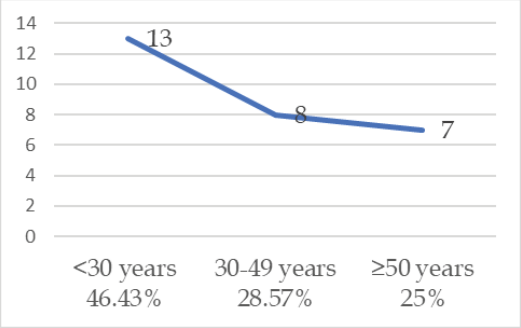

Figure 4. Distribution by age groups of patients included in the study

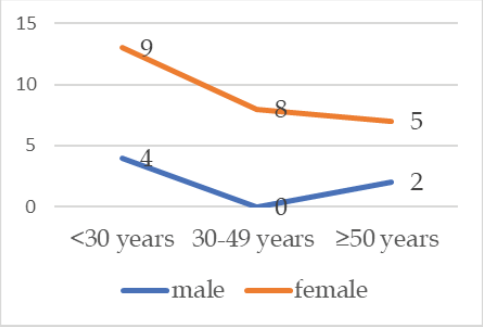

Figure 5. Distribution by age groups and sexes of patients included in the study

Of the 28 patients included in the sample, 6 patients (21.43%) presented wet post-extraction alveolitis, while 22 patients (78.57%) presented dry alveolitis.

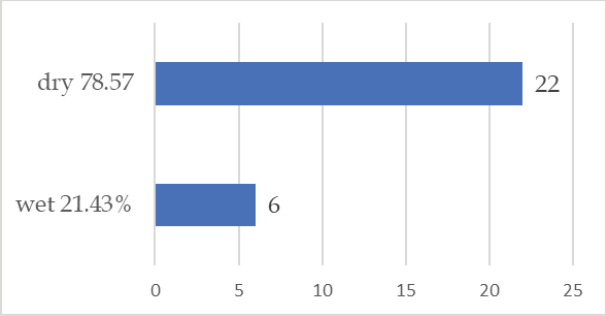

Figure 6. Distribution by type of post-extraction alveolitis

Depending on the number of dental units extracted, 24 patients (85.71%) developed post-extraction alveolitis after a single extraction, 3 patients (10.72%) after two extractions, and one patient (3.57%) among the 28 patients following the extraction of four dental units. In total, a number of 34 tooth extractions were performed (Figure 7).

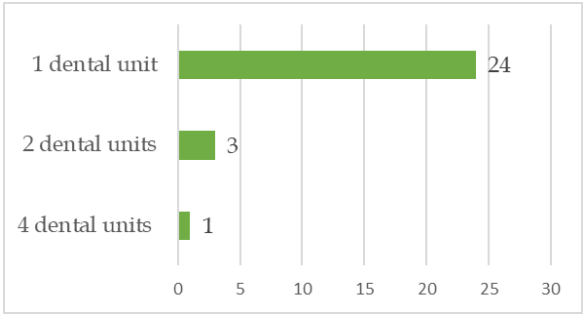

Figure 7. Distribution of patients according to the number of dental units extracted

From the point of view of the position of the extracted tooth, the lower molars represent the highest number of extractions.

From the 34 extractions performed on the 28 patients (Table 1), 22 of the extractions involved molars (64.71%), followed by 9 extractions of premolars (26.47%) and another 3 extractions of anterior teeth (8.82%). In total, 31 extractions of posterior teeth (91.18%). The extractions involving the mandibular third molar were 8 (36.36%) of the 22 molar extractions. Compared to the total of 34 extractions, the extractions of the mandibular third molar represent 23.53%.

Table 1. The distribution of extractions according to the position of the tooth

Position of the tooth		No. of extractions
Posterior	Premolar	9
	Molar	22
	Total	31
Anterior		3
Total		34

The patients presented post-extraction alveolitis predominantly at the mandibular level and are divided as follows: 21 patients (75%) presented mandibular alveolitis, 6 patients (21.43%) presented alveolitis at the level of the maxillary arch and only one case (3.57%) that presented alveolitis at both maxillary and mandibular level (Figure 8).

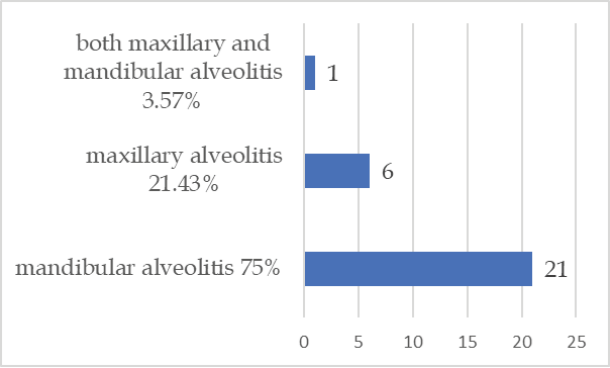

Figure 8. Location of post-extraction alveolitis

From all the extractions performed, 18 patients benefited from simple extractions (64.29%), and 10 patients (35.71%) required the application of surgical extraction techniques, as can be seen in Figure 9.

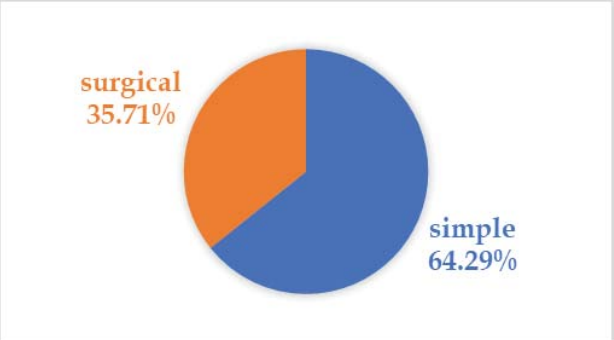

Figure 9. Distribution of patients according to the type of extraction

Also, from the total number of extractions, 7 patients (25%) required the administration of anesthetic in additional doses. In the case of these patients, the average anesthetic administered is 3 carpules.

Of the 28 patients, only one presented the dislocation of the adjacent tooth. Dental trauma and prolonged surgical time are factors that can lead to the development of post-extraction alveolitis.

Regarding the associated complications, a number of 8 patients (28.57%) presented acute cellulitis and 4 patients (14.29%) presented abscess. In total, 12 patients (42.86%) presented associated complications (Figure 10).

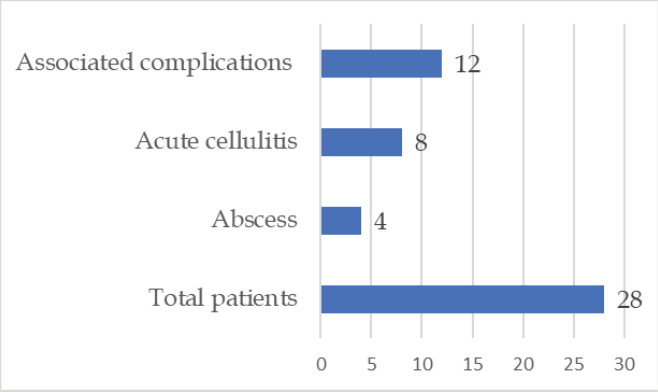

Figure 10. Complications associated with extractions

Regarding the comorbidities presented by the patients (Table2), they are classified according to nature into: cardiovascular-6 patients (21.43%), endocrine and metabolic-3 patients (10.71%), osteo-articular-2 patients (7.14%) and multiple–1 patient (3.57%).

Endocrine-metabolic diseases are represented by type II diabetes (one patient) and thyroid diseases (2 patients), and osteo-articular diseases by chronic osteitis and osteoporosis. The patient with multiple comorbidities presented hypothyroidism and grade II hypertension. In the case of cardiovascular diseases, the most frequent pathologies were myocardial ischemia and arterial hypertension. Also, 3 of these patients also presented anxiety disorders.

Table 2. **Distribution of patients according to comorbidities**

Comorbidity			No. of patients
Cardiovascular			6
Endocrine and metabolic	Type II diabetes	1	3
	Thyroid diseases	2	
Osteoarticular	Chronic osteitis		2
	Osteoporosis		
Multiple	Hypothyroidism and HTN		1

Smoking is one of the risk factors in the development of post-extraction alveolitis, although the mechanism by which it intervenes in the healing of the alveolus is still unclear. Of the 28 patients included in the studied group, 5 patients (17.86%) are smokers (Figure 11).

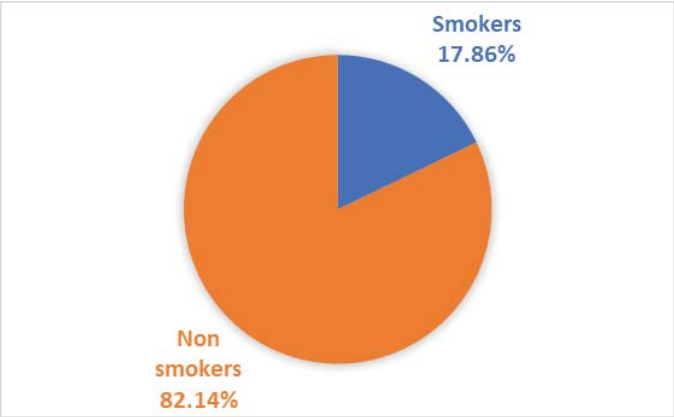

Figure 11. Distribution of patients according to tobacco consumption

From the point of view of the medication administered at the time of extraction, 2 patients (7.14%) were on anticoagulant/antiplatelet treatment, one patient (3.57%) under treatment with bisphosphonates and 4 patients (14.29%) under treatment oral contraceptive (Table 3).

Also, 2 of the studied patients (7.14%) are both smokers and follow chronic oral contraceptive treatment.

Table 3. **Treatment followed at the time of extraction**

Treatment	No. of patients
anticoagulant	1
antiplatelet agent	1
bisphosphonates	1
oral contraceptive	4

DISCUSSIONS

In the study, the percentage of female patients is higher (79%) than male patients (21%). This observation is explained by the literature by highlighting the hormonal differences between the two sexes, more precisely by the presence of estrogen. Even before the introduction of the oral contraceptive pill, the risk of female patients developing post-extraction alveolitis was higher according to studies, but it increased significantly for those using this method of pregnancy prevention. Estrogen is known to increase the production of coagulation factors II, VII, VIII and X, and in particular plasminogen, the precursor of plasmin – the main endogenous factor that leads to blood clot breakdown [1]. This shows how taking oral contraceptive pills can promote early clot breakdown by increasing local plasmin levels. In the female group of patients under study, 4 of them (14.29%) were taking contraceptive pills at the time of extraction. Some studies have also noted a relationship between alveolar osteitis and the stage of the menstrual cycle at which the extraction was performed and reported that the incidence is highest around cycle days 1 to 22 [1].

Although the literature supports the general axiom that the older the patient, the greater the risk of post-extraction alveolitis, this direction was not observed in the studied sample, the highest incidence being in the 18-29 age range (46, 43%), to decrease in percentage with increasing age. These results can be explained by the integrity of the alveolar bone and the low presence of periodontal diseases in the young population, which make the extraction more difficult [6].

It should be highlighted that in each sample made according to age, the percentage of female patients was higher, highlighting once again that the gender of the patient is a risk factor in the development of alveolar osteitis.

It is well documented in the literature that prolonged or particularly traumatic extractions have a higher incidence of post-extraction alveolitis [6]. By analogy, surgical extractions compared to non-surgical extractions have an increased risk of developing fibrinolytic alveolitis. Although in the present study only 35.71% presented alveolar osteitis following surgical extraction, the increased trauma can also be represented by other external factors such as the level of experience of the attending physician, intraoperative accidents, mandibular location and the need for a single extraction.

Bacterial presence has a negative role in the healing of the alveolus both by generating complications of an infectious nature associated with the extraction, and by the fibrinolytic activity exerted on the blood clot by certain bacterial enzymes [7]. Plasmin-like fibrinolytic activity was also observed in colonies of Treponema denticola, a microorganism present in periodontal infection [1]. *In vivo*, the fibrinolytic effect of bacterial pyrogens was highlighted [8]. Of all observed patients, 42.86% presented complications due to bacteria, respectively 14.29% presented abscess - purulent collection caused by the penetration of bacteria into sterile soft tissues under normal conditions, and 28.57% presented acute cellulitis - inflammatory condition what precedes the septic process. The increased presence of bacteria in the oral cavity is promoted by the lack of oral hygiene, another factor incriminating the formation of alveolar osteitis, to which can be added the non-observance of post-extraction food instructions, a series of fermented foods containing bacteria of the genus Bacillus that secrete fibrinolytic enzymes [7].

Related to tooth position, as expected, a significant incidence was observed in posterior tooth extractions (91.18%). Of the posterior teeth extracted, molars occupy the largest part (22 out of 31 extractions). Alveolar osteitis has been shown to be more common following mandibular third molar extraction [9,10]. Some authors believe that increased bone density, decreased vascularity, and reduced ability to produce granulation tissue are responsible for site specificity, although there is no evidence to suggest a link between fibrinolytic alveolitis and insufficient blood supply [1]. The specificity of the area is probably due to the high percentage of surgically extracted mandibular molars and may highlight the effect of trauma due to inaccessibility. Of the total extractions that developed post-extraction alveolitis, 23.53% are represented by the extraction of the mandibular third molar.

In most studies, the mandible is the most frequent site of alveolar osteitis, attributed to difficult and traumatic extractions [6]. From the analysis carried out per batch, the same trend of appearance of fibrinolytic alveolitis at the mandibular level emerged (75%).

Although multiple studies have shown that there is a link between smoking and post-extraction alveolitis, this aspect does not emerge from the data obtained, the percentage of smoking patients being only 17,86%. As the mechanism underlying the process is not fully elucidated, different hypotheses have been suggested that incriminate the high temperature of the inhaled smoke, the toxins it contains and the absorption action of the smoke that creates a negative intraoral pressure with the consequence of breaking the clot. This latter phenomenon is also found when drinking liquids with a straw [1].

The evidence indicating a higher prevalence of post-extraction alveolitis after single extractions compared to multiple extractions is limited, but this conclusion also emerged from the analyzed data, with 85.71% of patients requiring extraction treatment for a single dental unit. This difference could be due to the increased trauma in patients with single extractions compared to patients with multiple extractions whose teeth are damaged at a more advanced level, making the procedure less traumatic [9].

Many studies have shown a significant association between diabetes and alveolar osteitis, this pathology being characterized by lower immunity and delayed wound healing. Fibrinolytic alveolitis occurs due to disruption of blood flow, and in patients with diabetes the incidence is higher due to microangiopathy [11]. Among the observed patients, only one presented type II diabetes as a comorbidity. An increase in blood sugar level above the normal value of ≥126mg/dL could be considered a risk factor for post-extraction alveolitis both in patients with a history of diabetes and in those without this comorbidity [12].

Primary hypothyroidism is a condition characterized by the inability of the thyroid gland to produce enough thyroid hormones. Thyroid hormones play an important role in regulating the growth, development and metabolic functions of the body. Susceptibility to infection, delayed wound healing, and the complication of fibrinolytic alveolitis are common features of hypothyroidism, which may be due to decreased metabolic activity of fibroblasts and longer exposure of the wound to pathogenic organisms. Patients with hypothyroidism are more prone to developing cardiovascular diseases [13]. From the cases analyzed, only one patient classified as having multiple comorbidities presented both hypothyroidism and hypertension.

Anticoagulant patients requiring dental extractions face intraoperative and postoperative bleeding problems that may be difficult to control. If sufficient hemostasis is not achieved after oral surgery, complications such as post-extraction alveolitis, delayed healing and pain may occur [14]. In this study, one patient was being treated with oral anticoagulants. The goal of anticoagulant therapy is to prevent the formation or expansion of clots. Coumarin anticoagulants are vitamin K antagonists required for the synthesis of coagulation factors II, VII, IX and X, as well as endogenous anticoagulant proteins C and S [15].

Antiplatelet drugs are used to prevent arterial and venous thrombosis. In this study, one patient was undergoing antiplatelet treatment. Intra- and postoperative bleeding in patients receiving oral antithrombotic raises many problems, and withholding drug therapy to prevent complications is controversial [16].

Several protocols are used to minimize bleeding complications and to keep the patient's drug dose unchanged, such as suturing the wound or applying various local hemostatic agents [14].

Drug-induced osteonecrosis of the jaws with oral bisphosphonates can result in severe and extensive bone exposure and may require prolonged surgery, therefore patients taking oral bisphosphonates should be treated differently from patients not on this treatment. They are commonly prescribed to prevent complications in malignant bone diseases and in benign bone diseases such as osteoporosis. Only one patient in the study was taking this medication at the time of extraction, who was also diagnosed with osteoporosis. The mechanism by which bisphosphonates influence bone metabolism is not fully understood. However, they are potent inhibitors of osteoclast-mediated bone resorption, inhibit cell function, and induce early apoptosis. Because bisphosphonates have a very high affinity for hydroxyapatite crystals, they have the ability to localize and accumulate on bone mineral surfaces, particularly at sites of high bone turnover. Mammalian jaws are thought to have the ability to regenerate at a rate picked up [17]. Invasive dental procedures should be avoided whenever possible in patients with a history of bisphosphonate use, especially intravenous bisphosphonates for cancer. Discontinuation of oral and intravenous bisphosphonates is recommended before invasive dental procedures and after the development of osteonecrosis of the jaw, provided the systemic condition permits. Limited surgical debridement along with systemic and local antibiotics is the management of osteonecrosis of the jaw, however, cure is not assured [18].

CONCLUSIONS

Following the study carried out over a period of one year, several aspects related to post-extraction alveolitis were concluded.

The highest probability of development is found in young patients, under 30 years old. Due to hormonal differences, women are more prone than men, especially if they take oral contraceptive pills.

Posterior teeth show a higher frequency of development, of which the most numerous cases were represented by molars. The location of the extractions at the level of the mandible can be considered a risk factor because it involves a high trauma. Single extractions present a higher risk of formation due to the integrity and non-alteration of the alveolar bone.

The presence of bacteria can be considered one of the causes of the development of post-extraction alveolitis, but also of complications of bacterial etiology.

Although complications following surgical extractions were less frequent than in simple ones, they present high or prolonged trauma as a common factor.

Patients suffering from type II diabetes and hypothyroidism require additional monitoring due to the slow healing of the lesion. Patients under anticoagulant, antiplatelet and contraceptive treatment have an increased risk of developing fibrinolytic alveolitis. Although the literature supports smoking as a risk factor, in the analyzed data only 17.86% of the patients were smokers, the mechanisms involved in clot dislocation being unexplained.

REFERENCES

1. Veale B. Alveolar osteitis: a critical review of the aetiology and management. Oral Surgery. 2015; 8:68–77. https://doi.org/10.1111/ors.12130
2. Kolokythas A, Olech E, Miloro M. Alveolar osteitis: a comprehensive review of concepts and controversies. Int J Dent. 2010; 2010:249073. doi: 10.1155/2010/249073. Epub 2010 Jun 24. PMID: 20652078; PMCID: PMC2905714.
3. Kamal A, Salman B, Abdul Razak NH, Alqabbani A, Samsudin A. The Efficacy of Concentrated Growth Factor in the Healing of Alveolar Osteitis: A Clinical Study. International Journal of Dentistry. 2020;(6):1-9. 10.1155/2020/9038629.
4. Bucur A, Navarro Vila C, Lowry J, Acerosub J. Compendiu de chirurgie oro-maxilo-facială. Q Med Publishing. Vol 2. 2009.
5. Termeie DA. Avoiding and Treating Dental Complications Best Practices in Dentistry EDitED By. 2016.
6. Kumar S, Goyal R, Arora S, Kusum K. Assessment of Incidence and Risk Factors of Dry Socket. Int Arch BioMed Clin Res6. 2022Oct.28;8(1):DS1-DS3.
7. Almutairi BM. Dry sockets-a systemic review. 2019.
8. Hariharan R, Aravindha Babu N, Masthan KMK, Krupaa RJ. Alveolar Osteitis-A Review. 2020.
9. Kolokythas A, Olech E, Miloro M. Alveolar osteitis: a comprehensive review of concepts and controversies. Int J Dent. 2010; 2010:249073. doi: 10.1155/2010/249073. Epub 2010 Jun 24. PMID: 20652078; PMCID: PMC2905714.
10. Chandran S, Alaguvelrajan M, Karthikeyan A, Ganesan K, Faiz MK, Krishna Vallabhaneni SS. Incidence of Dry Socket in South Chennai Population: A Retrospective Study. 2016;8(1):119-122.
11. Prerana G, Tantry D, Sougata K, Sivalanka SC. Incidence of complications after the surgical removal of impacted mandibular third molars: A single centre retrospective study. J Acad Dent Educ 2021;7(1):10-7.
12. Hassan M, Karbassi A, Salehi R, Kheirollahi K, Targhi MG, Sadrabad MJ, Yousefipour B. The Relationship between Socket Blood Sugar and Post-Extraction Complications in Type II Diabetic and Non-Diabetic Patients. IJDO. 2015;7(1):12-19 URL: http://ijdo.ssu.ac.ir/article-1-225-en.html

13. Lone PA, Nargotra R, Rehman B, Singh M. Prevalence of Hypothyroidism in Females with Exodontia: A Randomized Prospective Study. International Journal of Scientific Study. 2015;3(8):31-34. doi. 10.17354/ijss/2015/503
14. Ragab HR, Melek LN. Comparison of two hemostatic agents in patients receiving anticoagulants without altering medication dosage. Egyptian Dental Journal. 2019;65(Issue 4 - October (Oral Surgery)): 3315-3321. doi: 10.21608/edj.2019.74763
15. Maani S, Saleh M, Melek L, Sadaka M. Evaluation of colloidal silver gelatin sponge (gelatamp) in patients receiving anticoagulant after tooth extraction (clinical study). Alexandria Dental Journal. 2015;40(1):101-106. doi: 10.21608/adjalexu.2015.58743
16. Brancaccio Y, Antonelli A, Barone S, Bennardo F, Fortunato L, Giudice A. Evaluation of local hemostatic efficacy after dental extractions in patients taking antiplatelet drugs: a randomized clinical trial. Clin Oral Investig. 2021 Mar;25(3):1159-1167. doi: 10.1007/s00784-020-03420-3. Epub 2020 Jul 1. PMID: 32613433.
17. Malden N, Beltes C, Lopes V. Dental extractions and bisphosphonates: the assessment, consent and management, a proposed algorithm. Br Dent J. 2009 Jan 24;206(2):93-8. doi: 10.1038/sj.bdj.2009.5. PMID: 19165270.
18. Borromeo GL, Tsao CE, Darby IB, Ebeling PR. A review of the clinical implications of bisphosphonates in dentistry. Aust Dent J. 2011 Mar;56(1):2-9. doi: 10.1111/j.1834-7819.2010.01283.x. Epub 2010 Dec 22. PMID: 21332734.