Journal of Population Therapeutics & Clinical Pharmacology

REVIEW ARTICLE
DOI: 10.53555/knke3341

PREVALENCE AND MANAGEMENT OF MEDICATION-RELATED OSTEONECROSIS OF THE JAW (MRONJ) IN PAKISTANI PATIENTS

Dr. Syeda Bushra Inayat[1*], Dr. Noor ul Fatima[2], Dr. Misbah Abbasi[3], Dr. Sualeha M. Qasim[4], Dr. Aqsa Wahid Ghauri[5], Dr. Bakhtawar Khan[6]

[1*]Lecturer, Department of Oral Biology, Dow International Dental College, Karachi
[2]Jinnah Sindh Medical University, Karachi
[3]Jinnah Sindh Medical University, Karachi
[4]Qasim Dental care sector 11-F, New Karachi, Karachi
[5]Lecturer, Anatomy Department, Dow International Dental College, Karachi
[6]Dental Care Clinic, Liaquatabad 4, Karachi

***Corresponding Author:** Dr. Syeda Bushra Inayat
*****Lecturer, Department of Oral Biology, Dow International Dental College, Karachi

Abstract

Background: Antiresorptive and antiangiogenic therapies may cause medication-related osteonecrosis of the jaw (MRONJ), which is a significant adverse effect.

Objective: To determine the prevalence and evaluate the current management practices of MRONJ among Pakistani patients.

Methodology: A descriptive cross-sectional study was conducted at Karachi Hospital over six months (January to June 2024). Non-probabilities 118 individuals at least 18 years old, with a history of using antiresorptive or antiangiogenic drugs, and with clinical characteristics indicative of MRONJ were recruited by easy sampling. Interviews, exams, and evaluations of medical records were used to gather information on demographics, underlying diseases, medication history, clinical staging, risk factors, and treatment strategies. SPSS v25 was used for statistical analysis, and chi-square tests were used to evaluate relationships ($p < 0.05$ significance).

Results: Among the patients, 48.31% were between the ages of 41 and 60, and 59.32% were female. The most prevalent underlying ailment was osteoporosis (54.24%), while the most common drug was denosumab (41.53%). The two biggest risk variables were recent dental extractions (56.78%) and poor oral hygiene (61.02%). Clinically, 27.12% had Stage 3 MRONJ and 43.22% had Stage 2 MRONJ. Surgical resection (16.95%), surgical debridement (30.51%), and conservative therapy (52.54%) were among the management techniques. Compared to conservative therapy (30.65%), surgical intervention demonstrated greater complete recovery rates (55.36%). Age ($p=0.001$), length of medication usage ($p=0.003$), tooth extraction history ($p<0.001$), and diabetes mellitus ($p=0.046$) were all significantly associated with advanced MRONJ stages.

Conclusion: MRONJ is prevalent among Pakistani patients with antiresorptive therapy, with surgical management yielding better outcomes than conservative methods.

Keywords: Osteoporosis, Medication-related osteonecrosis of the jaw, Bisphosphonates, Denosumab.

Introduction

Medication-related osteonecrosis of the jaw (MRONJ), a side effect that is becoming more well recognized, is associated with the use of antiresorptive and antiangiogenic medications, particularly denosumab and bisphosphonates [1].

These medications are often used to treat osteoporosis, metastatic bone disease, and multiple myeloma [2].

Their long-term usage has been associated with negative effects on jawbone health, despite the fact that they provide significant advantages in lowering skeletal-related occurrences [3].

In individuals with a history of relevant pharmaceutical usage but no history of radiation treatment to the jaws, MRONJ is defined by exposed necrotic bone in the maxillofacial area that lasts longer than eight weeks [4].

Globally, the frequency of MRONJ varies according on a number of variables, including genetic predispositions, dental surgeries, length of treatment, medication type, and mode of administration [5]. However, the full impact of MRONJ is still not well understood in low-income nations due to a lack of awareness, delayed diagnosis, and uneven reporting procedures [6].

Poor results for afflicted individuals are also a result of the reactive rather than preventative nature of dental treatment and the lack of multidisciplinary contact between endocrinologists, oncologists, and dentists [7].

From minor pain and localized swelling to severe infection and pathological fractures, MRONJ may present with a variety of clinical symptoms [8]. Depending on the stage and severity of the illness, treatment techniques may include more invasive procedures like surgical debridement or resection, or more conservative ones such antibacterial mouth rinses and antibiotics [9,10].

Patient comorbidities and the continuous need for antiresorptive medication further complicate treatment decisions, requiring a careful balancing act between maintaining oral health and controlling systemic illness [11].

Effective management is made more difficult in the Pakistani healthcare system by patient non-compliance, inadequate physician training, and a lack of defined treatment regimens. The disease's course may be accelerated by cultural and financial hurdles that impede prompt access to necessary dental treatment. These difficulties show how important it is to have accurate information on the prevalence and current treatment methods of MRONJ in the community in order to guide future therapeutic recommendations and educational initiatives.

Research Objective

To determine the prevalence and evaluate the current management practices of MRONJ among Pakistani patients.

Methodology

Study Design and Setting

This descriptive cross-sectional study was conducted at the Department of Oral Biology, Karachi Hospital, over a period of six months, from January 2024 to June 2024.

Inclusion and Exclusion Criteria

Participants required to be at least 18 years old and, regardless of gender, had to have a history of using antiresorptive or antiangiogenic drugs (e.g., denosumab or bisphosphonates) for osteoporosis, metastatic bone disease, or multiple myeloma. Only patients with a history of radiation therapy to the jaws and clinical symptoms consistent with MRONJ—defined as exposed bone in the maxillofacial region that has lasted for more than eight weeks—were included in the study. Patients having a history of radiation therapy to the head and neck region or those with traumatic bone exposures unrelated to drug use were excluded.

Sample Size
A total of 118 patients were enrolled using a non-probability convenient sampling technique. All eligible patients presenting to the hospital during the study period were approached for participation.

Data Collection
Structured interviews, clinical examinations, and medical record reviews were used to gather data. Demographic information, the type and length of antiresorptive/antiangiogenic drug usage, the clinical presentation of MRONJ, dental operation history, the stage of MRONJ at diagnosis, and the therapeutic strategy (conservative vs. surgical) were among the data collected. To guarantee uniformity, a consistent data collecting form was used.

Statistical Analysis
The collected data was entered and evaluated using SPSS version 25. Descriptive statistics were calculated for clinical parameters and demographic data, including frequencies, percentages, averages, and standard deviations. The associations between the variables were assessed using the Chi-square test where appropriate; a p-value of less than 0.05 was considered statistically significant.

Results
As shown in table 1, of the 118 patients with a diagnosis of MRONJ, the majority were female (n = 70, 59.32%), whereas 40.68% were male (n = 48). The majority of patients (n = 57, 48.31%) were between the ages of 41 and 60, followed by those over 60 (n = 39, 33.05%), and those between the ages of 18 and 40 (n = 22, 18.64%).

Table 1: Demographic Characteristics of Patients with MRONJ (n = 118)

Variable	Category	Frequency (n)	Percentage (%)
Gender	Male	48	40.68
	Female	70	59.32
Age Group (Years)	18–40	22	18.64
	41–60	57	48.31
	>60	39	33.05

According to table 2, osteoporosis was the most prevalent underlying illness among MRONJ patients (n = 64, 54.24%), followed by multiple myeloma (n = 15, 12.71%) and metastatic bone disease (n = 39, 34.05%). 41.53% (n = 49) of patients utilized denosumab, while 34.75% (n = 41) and 23.73% (n = 28) of patients had used oral and intravenous bisphosphonates, respectively. Most patients (n = 52, 44.07%) had been taking their medications for one to three years, then more than three years (n = 47, 39.83%), and less than one year (n = 19, 16.10%).

Table 2: Underlying Conditions and Medication History (n = 118)

Variable	Category	Frequency (n)	Percentage (%)
Primary Condition	Osteoporosis	64	54.24
	Metastatic Bone Disease	39	33.05
	Multiple Myeloma	15	12.71
Type of Medication	Bisphosphonates (Oral)	41	34.75
	Bisphosphonates (IV)	28	23.73
	Denosumab	49	41.53
Duration of Medication Use	<1 year	19	16.10
	1–3 years	52	44.07
	>3 years	47	39.83

Poor oral hygiene was the most common risk factor, affecting 61.02% (n = 72) of patients, as seen in figure 1. 32.20% (n = 38) reported using dentures, while 56.78% (n = 67) claimed having a recent history of dental extractions. Furthermore, 24.58% (n = 29) had a history of smoking, and 29.66% (n = 35) had diabetes mellitus. Interestingly, patients often had several risk factors.

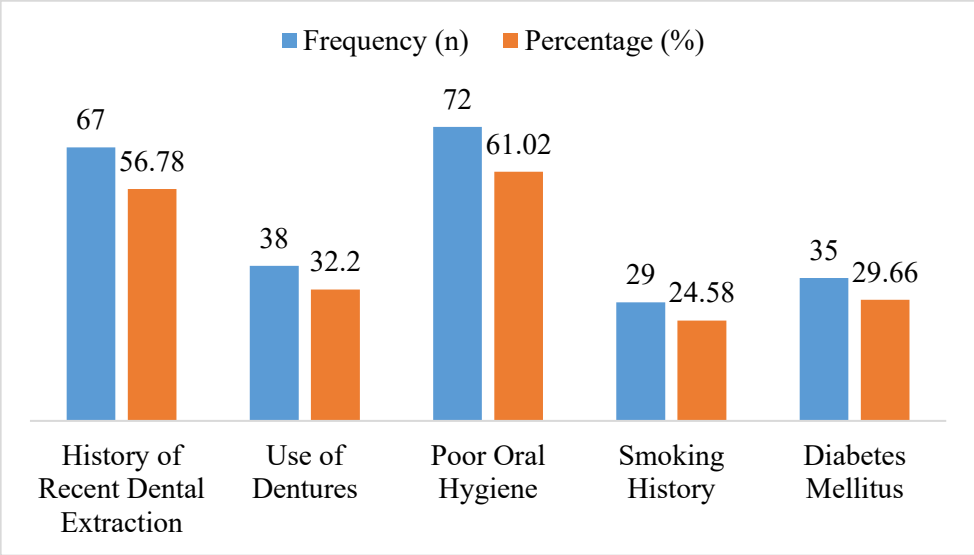

Figure 1: Dental History and Risk Factors (n = 118)

There was a significant percentage of advanced-stage cases at diagnosis, as shown by the majority of patients presenting with Stage 2 MRONJ (n = 51, 43.22%), followed by Stage 3 (n = 32, 27.12%), Stage 1 (n = 27, 22.88%), and Stage 0 (n = 8, 6.78%) (figure 2).

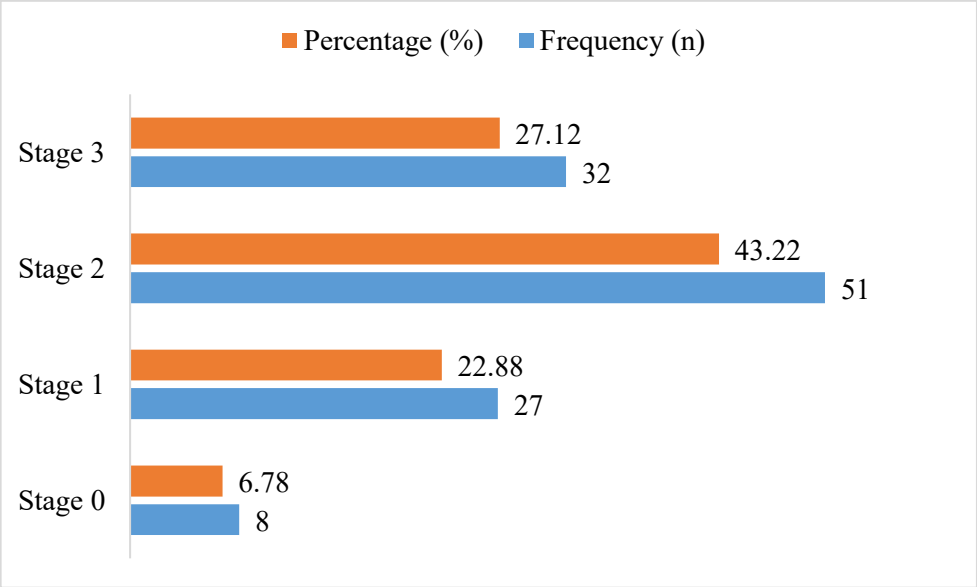

Figure 2: Clinical Presentation and Staging of MRONJ (n = 118)

Oral rinses and antibiotics were used in 52.54% (n = 62) of patients as part of conservative therapy. The requirement for intrusive methods in advanced illness is shown by the fact that 30.51% (n = 36) had surgical debridement and 16.95% (n = 20) underwent surgical resection (figure 3).

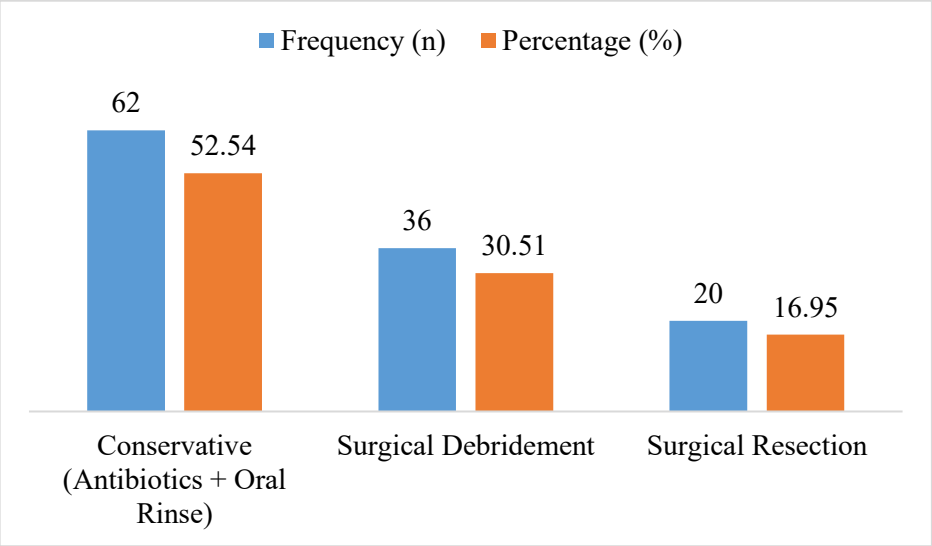

Figure 3: Management Strategies Used in MRONJ Patients (n = 118)

In contrast to 55.36% (n = 31) in the surgical group (n = 56), 30.65% (n = 19) of patients undergoing conservative therapy (n = 62) had a complete recovery. 53.23% (n = 33) of patients treated conservatively and 33.93% (n = 19) of patients treated surgically showed some improvement. 10.71% (n = 6) of surgical cases and 16.13% (n = 10) of conservative cases showed no improvement, indicating that surgical procedures produced better results (table 3).

Table 3: Treatment Outcome by Management Type (n = 118)

Outcome	Conservative (n=62)	Surgical (n=56)	Total (n=118)
Full Recovery	19 (30.65%)	31 (55.36%)	50 (42.37%)
Partial Improvement	33 (53.23%)	19 (33.93%)	52 (44.07%)
No Improvement	10 (16.13%)	6 (10.71%)	16 (13.56%)

Age group (p = 0.001), length of medication usage (p = 0.003), history of tooth extraction (p < 0.001), and diabetes mellitus (p = 0.046) all showed significant relationships with advanced MRONJ (Stage 2-4). There were no significant connections between gender and drug type (p = 0.328 and p = 0.642, respectively). In severe phases, comorbid diseases, advanced age, and prolonged drug use were more prevalent (table 4).

Table 4: Association Between Clinical and Demographic Variables and MRONJ Severity (n = 118)

Variable	Category	Stage 0–1 (n=35)	Stage 2–3 (n=83)	*p*-value
Gender	Male	19	29	0.328
	Female	16	54	
Age Group (Years)	18–40	12	10	0.001
	41–60	18	39	
	>60	5	34	
Medication Type	Bisphosphonates (Oral/IV)	21	48	0.642
	Denosumab	14	35	
Duration of Medication	<1 year	10	9	0.003
	1–3 years	19	33	
	>3 years	6	41	
Dental Extraction History	Yes	12	55	<0.001
	No	23	28	
Diabetes Mellitus	Present	6	29	0.046
	Absent	29	54	

Discussion

The prevalence, risk factors, clinical staging, and treatment techniques of MRONJ in a Pakistani community are all well-explained by this research. In line with other studies showing a higher frequency of MRONJ in women due to increased use of antiresorptive treatment for postmenopausal osteoporosis, women made up a larger percentage of the 118 diagnosed cases (59.32%) than men (40.68%) [12]. In line with results from earlier regional studies that showed middle-aged and elderly patients made up the bulk of MRONJ cases, the most afflicted age group was 41–60 years old (48.31%) [13].

In 54.24% of cases, osteoporosis was the main ailment, followed by multiple myeloma (12.71%) and metastatic bone disease (34.05%). This is consistent with research showing that the most common reason for bisphosphonate or denosumab treatment in MRONJ patients is osteoporosis [14]. The most often implicated agent was denosumab (41.53%), which was followed by intravenous bisphosphonates (23.73%) and oral bisphosphonates (34.75%). This is in contrast to previous studies that found intravenous bisphosphonates to be the most common [15], which may indicate a change in prescription habits or variations in local medication availability.

The most common risk factors were recent dental extractions (56.78%) and poor oral hygiene (61.02%). These results support previous research showing that poor oral hygiene and invasive dental treatments are important factors in the pathophysiology of MRONJ [16]. Additionally, diabetes mellitus was present in 29.66% of patients, and this condition was substantially linked to advanced MRONJ stages ($p = 0.046$). This is in line with claims that diabetes increases vulnerability to osteonecrosis and hinders wound healing [17].

In terms of clinical prevalence, Stage 2 MRONJ was most prevalent (43.22%), followed by Stage 3 (27.12%), suggesting that many patients had advanced illness when they first arrived. Similar trends have been seen in other low-resource environments, where disease development is facilitated by delayed diagnosis and restricted access to dental treatment [18].

52.54% of patients had conservative treatment, 30.51% underwent surgical debridement, and 16.95% underwent resection. Results were better in the surgical group, with 55.36% of patients fully recovering, compared to 30.65% in the conservatively treated group. This confirms results from earlier studies that suggest surgery for advanced MRONJ, particularly in cases when conservative treatments are ineffective [19]. It's interesting to note that more severe disease stages were linked to longer pharmaceutical usage (>3 years) ($p = 0.003$), supporting earlier findings that linked extended antiresorptive treatment to a higher risk of MRONJ [20].

Study Strengths and Limitations

This research fills a major gap in the regional literature by providing thorough information on the prevalence, risk factors, clinical presentation, and therapeutic results of MRONJ in a Pakistani population. The results' dependability and generalizability in comparable healthcare settings are improved by the use of systematic data collecting techniques and a comparatively large sample size (n=118). Furthermore, the examination of correlations between clinical factors and the severity of the illness provides important information for risk assessment and treatment choices. The single-center design is one of the disadvantages, however, since it would restrict how broadly the findings can be applied across Pakistan. Selection bias may be introduced when non-probability convenience sampling is used. Furthermore, the study's cross-sectional design limits the capacity to determine long-term treatment results or causal links. Further multicenter longitudinal research is necessary to confirm these results and evaluate the long-term effects of various treatment approaches.

Conclusion

According to this research, MRONJ is a serious side effect that mostly affects middle-aged to older individuals and women in Pakistan who are undergoing antiresorptive or antiangiogenic treatments. Denosumab is the most often utilized involved medicine, and osteoporosis continues to be the most common underlying disease. With a significant percentage of patients presenting at late stages of the illness, poor oral hygiene and tooth extractions are the main risk factors. When compared to

conservative methods, surgical care shows better recovery results, highlighting the need of early diagnosis and individualized treatment plans. These results highlight the value of interdisciplinary cooperation and raised awareness to enhance MRONJ prevention, prompt diagnosis, and efficient care in the community.

References

1. King R, Tanna N, Patel V. Medication-related osteonecrosis of the jaw unrelated to bisphosphonates and denosumab—a review. Oral surgery, oral medicine, oral pathology and oral radiology. 2019 Apr 1;127(4):289-99. https://doi.org/10.1016/j.oooo.2018.11.012.
2. AlDhalaan NA, BaQais A, Al-Omar A. Medication-related osteonecrosis of the jaw: a review. Cureus. 2020 Feb 10;12(2). DOI: 10.7759/cureus.6944.
3. Otto S, Pautke C, Van den Wyngaert T, Niepel D, Schiødt M. Medication-related osteonecrosis of the jaw: Prevention, diagnosis and management in patients with cancer and bone metastases. Cancer treatment reviews. 2018 Sep 1;69:177-87. https://doi.org/10.1016/j.ctrv.2018.06.007.
4. Yarom N, Shapiro CL, Peterson DE, Van Poznak CH, Bohlke K, Ruggiero SL, Migliorati CA, Khan A, Morrison A, Anderson H, Murphy BA. Medication-related osteonecrosis of the jaw: MASCC/ISOO/ASCO clinical practice guideline. Journal of Clinical Oncology. 2019 Sep 1;37(25):2270-90. https://doi.org/10.1200/JCO.19.01186.
5. Lorenzo-Pouso AI, Bagán J, Bagán L, Gándara-Vila P, Chamorro-Petronacci CM, Castelo-Baz P, Blanco-Carrión A, Blanco-Fernández MÁ, Álvarez-Calderón Ó, Carballo J, Pérez-Sayáns M. Medication-related osteonecrosis of the jaw: a critical narrative review. Journal of Clinical Medicine. 2021 Sep 24;10(19):4367. https://doi.org/10.3390/jcm10194367.
6. Coropciuc R, Moreno-Rabié C, De Vos W, Van de Casteele E, Marks L, Lenaerts V, Coppejans E, Lenssen O, Coopman R, Walschap J, Nadjmi N. Navigating the complexities and controversies of medication-related osteonecrosis of the jaw (MRONJ): a critical update and consensus statement. Acta Chirurgica Belgica. 2024 Jan 2;124(1):1-1. https://doi.org/10.1080/00015458.2023.2291295
7. Sturrock A, Preshaw PM, Hayes C, Wilkes S. General dental practitioners' perceptions of, and attitudes towards, improving patient safety through a multidisciplinary approach to the prevention of medication-related osteonecrosis of the jaw (MRONJ): a qualitative study in the North East of England. BMJ open. 2019 Jun 1;9(6):e029951. http://orcid.org/0000-0002-3316-1412.
8. Haviv Y, Geller Z, Mazor S, Sharav Y, Keshet N, Zadik Y. Pain characteristics in medication-related osteonecrosis of the jaws. Supportive Care in Cancer. 2021 Feb;29:1073-80. https://doi.org/10.1007/s00520-020-05600-z.
9. Varoni EM, Lombardi N, Villa G, Pispero A, Sardella A, Lodi G. Conservative management of medication-related osteonecrosis of the jaws (MRONJ): a retrospective cohort study. Antibiotics. 2021 Feb 17;10(2):195. https://doi.org/10.3390/antibiotics10020195
10. Vanpoecke J, Verstraete L, Smeets M, Ferri J, Nicot R, Politis C. Medication-related osteonecrosis of the jaw (MRONJ) stage III: Conservative and conservative surgical approaches versus an aggressive surgical intervention: A systematic review. Journal of Cranio-Maxillofacial Surgery. 2020 Apr 1;48(4):435-43. https://doi.org/10.1016/j.jcms.2020.02.017
11. Campisi G, Mauceri R, Bertoldo F, Bettini G, Biasotto M, Colella G, Consolo U, Di Fede O, Favia G, Fusco V, Gabriele M. Medication-related osteonecrosis of jaws (MRONJ) prevention and diagnosis: Italian consensus update 2020. https://doi.org/10.3390/ijerph17165998.
12. Ishimaru M, Ono S, Morita K, Matsui H, Hagiwara Y, Yasunaga H. Prevalence, incidence rate, and risk factors of medication-related osteonecrosis of the jaw in patients with osteoporosis and cancer: a nationwide population-based study in Japan. Journal of Oral and Maxillofacial Surgery. 2022 Apr 1;80(4):714-27. https://doi.org/10.1016/j.joms.2021.12.007.
13. Bracchi P, Zecca E, Brunelli C, Miceli R, Tinè G, Maniezzo M, Lo Dico S, Caputo M, Shkodra M, Caraceni AT. A real-world study on the prevalence and risk factors of medication related osteonecrosis of the jaw in cancer patients with bone metastases treated with Denosumab. Cancer Medicine. 2023 Sep;12(17):18317-26. https://doi.org/10.1002/cam4.6429.

14. Bagan J, Peydró A, Calvo J, Leopoldo M, Jiménez Y, Bagan L. Medication-related osteonecrosis of the jaw associated with bisphosphonates and denosumab in osteoporosis. Oral diseases. 2016 May;22(4):324-9. https://doi.org/10.1111/odi.12447.
15. Feng Z, An J, He Y, Zhang Y. A comparative study of the clinical characteristics of patients with medication-related osteonecrosis of the jaw and osteoporosis or malignancy. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology. 2022 Nov 1;134(5):543-7. https://doi.org/10.1016/j.oooo.2022.04.049.
16. Otto S, Aljohani S, Fliefel R, Ecke S, Ristow O, Burian E, Troeltzsch M, Pautke C, Ehrenfeld M. Infection as an important factor in medication-related osteonecrosis of the jaw (MRONJ). Medicina. 2021 May 9;57(5):463. https://doi.org/10.3390/medicina57050463.
17. Ruggiero BL, Edwards SP. Diabetes mellitus and its association with infection and osteonecrosis of the jaw. InDiabetes Mellitus 2020 Jan 1 (pp. 159-181). Academic Press. https://doi.org/10.1016/B978-0-12-820605-8.00008-5.
18. Lorenzo-Pouso AI, Bagán J, Bagán L, Gándara-Vila P, Chamorro-Petronacci CM, Castelo-Baz P, Blanco-Carrión A, Blanco-Fernández MÁ, Álvarez-Calderón Ó, Carballo J, Pérez-Sayáns M. Medication-related osteonecrosis of the jaw: a critical narrative review. Journal of Clinical Medicine. 2021 Sep 24;10(19):4367. https://doi.org/10.3390/jcm10194367.
19. Seluki R, Seluki M, Vaitkeviciene I, Jagelaviciene E. Comparison of the effectiveness of conservative and surgical treatment of medication-related osteonecrosis of the jaw: a systematic review. Journal of Oral & Maxillofacial Research. 2023 Dec 31;14(4):e1. doi: 10.5037/jomr.2023.14401.
20. Suryani IR, Ahmadzai I, Shujaat S, Ma H, Jacobs R. Non-antiresorptive drugs associated with the development of medication-related osteonecrosis of the jaw: a systematic review and meta-analysis. Clinical Oral Investigations. 2022 Mar 1:1-1. https://doi.org/10.1007/s00784-021-04331-7.