



Original Research Article

## Evaluation of awareness and knowledge about medication-related osteonecrosis of jaws among interns and postgraduates: A cross-sectional study

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### ABSTRACT

**Objectives:** Osteonecrosis is a common terminology used nowadays associated with severe trauma. Osteonecrosis also known as avascular necrosis occurs due to diminished blood supply, depriving bone tissue of essential nutrients, and oxygen leading to death of bone cells in a circumscribed region. Medication-related osteonecrosis of jaws (MRONJs) are a recent concept and correspond to necrosis of bones particularly jaw bones due to use of certain medications without any prior exposure to radiation. Several medications tend to alter the bone remodeling process, affecting the diseased bone resorption, and leading to poor oral health maintenance. Adequate documentation and awareness about this condition can help to prevent the condition. This study aims to evaluate the existing knowledge that prevails about pathogenesis, staging, and treatment modalities currently available about the condition among interns and postgraduates.

**Materials and Methods:** An online questionnaire-based cross-sectional survey was carried out among interns and postgraduates of VSPM's Dental College and Research Center. General characteristics, knowledge about medications responsible, pathogenesis, risk factors, staging, treatment protocols, and drug holiday were recorded that the responses were compiled and statistically analyzed.

**Results:** A total of 125 participants participated in the survey. About 72.8% of participants had heard about this condition earlier, whereas 8.8% were unaware of this terminology. About 27.2% people had no idea about the drug holiday concept. Furthermore, significant difference existed between designation and responses.

**Conclusion:** The results suggest that a significant difference exists between awareness about MRONJ among interns and postgraduates. Postgraduate students currently pursuing their degree were more aware and had significant knowledge about the clinical entity and more inclined toward further upgrading their knowledge about the same rather than interns.

**Keywords:** Medication-related osteonecrosis of jaws, Drug holiday, Anti-osteoporotic, Interns, Postgraduates, Bisphosphonates

### INTRODUCTION

Medication-related osteonecrosis of jaws (MRONJs) are debilitating clinical entity characterized by non-healing exposed bone associated with the use of anti-osteoporotic drugs primarily bisphosphonates without any prior exposure to radiation in the head and neck region. It refers to progressive bone death. It is an uncommon side effect seen in some individuals.

Marx, in 2003, reported the first instance of the condition as a side effect in a patient receiving bisphosphonate treatment.<sup>[1,2]</sup> Therefore, earlier this entity was known as BRONJ, bisphosphonate-related osteonecrosis of jaws. An update was made in 2014 by AAOMS to change the term from BRONJ to MRONJ following many case reports of

progressive bone death associated with anti-angiogenic and anti-resorptive drugs usage.<sup>[1]</sup> The prevalence of disease is very low, but its likelihood in cancer patients is 0–12%.

Several drugs have an impact on the bone loss process. These bone modifying drugs can lead to MRONJ. MRONJ is seen to be associated with anti-osteoporotic, anti-angiogenic drugs, and anti-resorptive drugs such as bisphosphonates and denosumab, selective estrogen receptors, and RANKL but more commonly is seen to be associated with bisphosphonates and denosumab which are also the two most frequently prescribed drugs for osteoporosis.<sup>[1]</sup>

Pathogenesis of the condition is not entirely understood till now but also it is hypothesized that the drugs interferes with

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osteoclast activity, altering the bone healing and remodeling process. Furthermore, they also inhibit angiogenesis. Tooth extraction and dentoalveolar surgeries are considered to be significant risk factors for MRONJ to develop.<sup>[1]</sup> The clinical evidence of necrotic bone for more than 8 weeks without healing is an indicator for the disease.

The side effects of bisphosphonate on bones even after discontinuation of the drug are an important reason to consider “DRUG HOLIDAY” for 3–5 years in patients on long-term bisphosphonates therapy. Drug holiday is not necessary for patients on denosumab as their effects do not persist after discontinuation.<sup>[1]</sup>

Since the necrotic effects of bone have not been observed outside bones of craniofacial region, dentists are essential in diagnosis and prevention of this entity this emphasizes the need to spread awareness among dental professionals. Treatment modalities are continuously being upgraded and newer research is being done on the topic. Therefore, it is essential that the future dental surgeons are aware and prepared to handle the condition and provide a better treatment protocol to their patients. The overarching aim of this study is to enhance knowledge of the dental professionals and draw their attention for further research about treatment protocols and newer advancements in this field.

### Aims and objectives

This study aims to evaluate the existing knowledge that prevails about pathogenesis, staging, and treatment modalities currently available about the condition among interns and postgraduates and whether they are aware of the serious complications of the condition.

### MATERIALS AND METHODS

A cross-sectional study was conducted in VSPM’s Dental College and Research Center among interns and postgraduates. Ethical clearance was obtained from the Institutional Ethics Committee of VSPM’s Dental College and Research Center; approved no IEC/VSPMDCRC/76/2022. A total of 125 participants participated in the study among which 96 were interns and 29 participants were postgraduate students studying in the VSPM educational academy campus. An online self-administered questionnaire was circulated from the month of June to August, and after recording 125 responses, the link was closed. Data collection was done from all the willing participants. The questionnaire recorded the demographic data, medications responsible, frequency of involvement, pathogenesis, staging, drug holiday administered, and treatment modalities available about the clinical entity. Data were collected using Google forms and were compiled in Excel Sheet and statistically analyzed using IBM SPSS 2020 Software. Test of significance used was Chi-square test to compare the values between the two groups.

### RESULTS

A total of 125 responses were collected. Range of age of the participants was between 22 and 28 years. Mean age was 23 years [Figure 1]. Among these 71.2% were female and the rest 28.8% were male [Figure 2]. About 76.8% of responses were recorded from interns and 23.2% of responses were from postgraduate group [Figure 3].

A descriptive analysis is depicted in [Table 1] below:

About 62.4% of students were aware about all the drugs causing osteonecrosis, whereas 20.8% of participants were only aware of bisphosphonates drug causing osteonecrosis. About 8.8% responders voted for denosumab and 8% of them thought that it is a side effect of anti angiogenic drugs. About 56% of students were in favor of mandibular involvement, whereas 16% favored maxillary involvement. About 13.6% of students were however not aware about which jaw bone was more affected and 14.4% of responders took a toll with equal in both the jaws.

About 36.8% of participants responded inhibition of osteoclast differentiation as a pathogenesis, 32% of participants favored inhibition of osteoblast differentiation as pathogenesis involved, 22.4% of participants responded with interference in bone remodeling, and 8.8% of individuals favored angiogenesis.

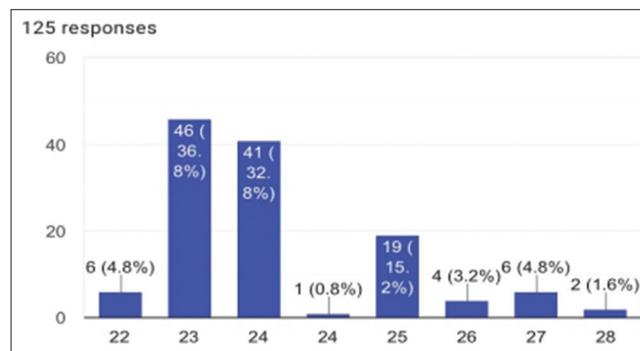


Figure 1: Age of participants.

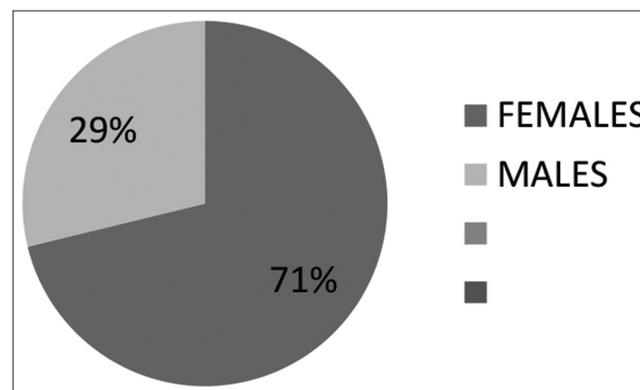


Figure 2: Gender of participants.

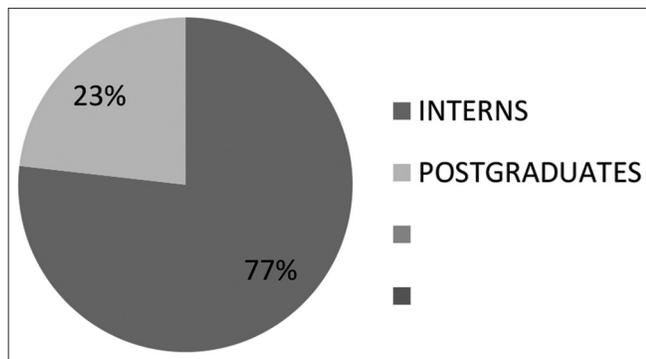


Figure 3: Designation of participants.

**Table 1: Gender and designation demographics.**

Descriptive statistics: Demographics		
	Frequency	Percent
Gender		
Female	89	71.2
Male	36	28.8
Total	125	100.0
Designation		
Intern	96	76.8
Postgraduate	29	23.2
Age		
Mean±SD: 23.96±1.24		

About 37.6% of participants were aware of the staging criteria used that are four stages existed for the condition, while 31.2% of participants responded that clinical entity consist of three staging system. A large population of 24.8% of participants, however, were not aware of the staging criteria, and 6.4% of participants responded to two stages.

Only 38.4% of students knew the drug holiday concept and the recommended drug holiday prescribed, while 10.4% people, 27.2% of participants had no idea about the concept of drug holiday. About 24% of population thought that drug holiday referred to non-availability of drug.

About 35.2% of students responded to >8 weeks duration for MRONJ to occur, 24.8% of students were not aware about the duration of MRONJ to occur, and 18.5% of responders responded with 5 weeks of duration, while the rest 21.6% responded 3 weeks.

About 69.9% of responders took a toll with all of the given options, while 13.6% of participants responded cancer or osteoporosis treatment as a risk factor. About 9.6% of participants answered dental implants to be a risk factor and rest 7.2% of participants favored tooth extractions.

About 55.2% of participants responded that the healing of extraction wound is affected in MRONJ cases, while 35.2% of participants were not sure about the affect and 9.6% of participants responded that it does not affect the wound healing process.

About 36% of student responses recorded clinical evidence of necrotic bone as a mainstay of diagnosis, 25.6% of individuals responses recorded non-healing extraction wound for >8 weeks, and 20.8% of individuals responded to radiography, while the rest 17.6% responded to biopsy.

About 65.6% of participants were in favor of surgical as well as conservative treatment modality, 20.8% of participants were not aware of the treatment modalities available, 8.8% of participants favored surgical intervention only, and 4.8% of participants responded with conservative management.

About 38.8% of students responded that surgical intervention is necessary in stages 2 and 3, 26.8% of students responded that surgical intervention is needed in all the stages, and 22.4% of students responded to surgical intervention in stage 3, while the rest 12.8% responded to intervention in stage 2.

Highest response for drug of choice for entity was recorded for metronidazole 40%. About 38.4% of participants responded with penicillin as drug of choice, 12.8% of students responded with clindamycin, and the rest 8.8% of students responded macrolides.

## DISCUSSION

This study focuses on the awareness and difference in levels of knowledge between interns and postgraduates. Medication-related osteonecrosis is sequelae which may occur after tooth extraction a most commonly carried out procedure in dentistry, leading to non-healing of extractions wounds. Bisphosphonates and non-bisphosphonates like medications are widely used in management of bone cancer and diseases,<sup>[2]</sup> and patients on these drugs are at high risk to develop osteonecrosis. Osteonecrosis or avascular necrosis is nor a specific disease entity, bur rather a condition leading to death of bone tissue in circumscribed region.<sup>[3]</sup> Therefore, it is necessary to evaluate whether or not awareness and proper treatment protocols are known to future clinicians and bring about their attention toward this clinical entity so that they can promptly identify the patients at risk and efficiently manage the condition. Although, the prevalence is lower than 12% with increasing rise in the administration of these drugs, the prevalence can be suspected to be increased.

A significant difference existed between the knowledge and perceptions of this clinical entity among interns and postgraduates. The response rate of our study was 100% as compared to 46.8% as recorded by Patil *et al.*<sup>[2]</sup> About 72.8% of participants had heard about the term MRONJ and aware about the clinical entity. No difference in the awareness about term was observed between intern and postgraduate group. However, the past studies observed that specialized dentists had better understanding.

In the study, awareness of MRONJ among dental professionals: A multicenter study, author recorded that only 31.6% of the participants were aware about the drug holiday concept.<sup>[2]</sup> However, 38.4% of participants were aware about the concept in our study which signifies the increase in awareness of the dental professionals. Furthermore, among interns and

postgraduates, 62% of participants of the postgraduate were aware and only 31.2% were aware among the interns group ( $P = 0.010$ ) [Table 2]. Similarly, 69.9% of participants of our study were well acquainted with the risk factors, while only 38.5% of the participants were aware in the previous study.<sup>[2]</sup> Difference between the knowledge among interns and postgraduates was also noted ( $P = 0.004$ ), [Table 3].

Similarly, difference in the knowledge and awareness was noted while recording staging ( $P = 0.000$ ), duration of MRONJ, diagnosis criteria, treatment modalities surgical intervention, and drug choice [Table 3].

It is important that along with dentist, medical professionals should also consider the risk factors while prescribing these medications.<sup>[2]</sup> Patients are mostly unaware of the drugs

**Table 2:** Interns and post graduates awareness about MRONJ.

Descriptive Statistics: Responses		
Questionnaire	Frequency	Percent
Are you aware of medication-related osteonecrosis of jaws?		
Never heard	11	8.8
No	23	18.4
Yes	91	72.8
Which drugs can cause medication-related osteonecrosis?		
Antiangiogenic drugs	10	8.0
Bisphosphonates	26	20.8
Denosumb	11	8.8
All of the above	78	62.4
Which jaw it affects more?		
Equal frequency in both	18	14.4
Mandible	70	56.0
Maxilla	20	16.0
Not aware	17	13.6
Pathogenesis is related to		
Angiogenesis	11	8.8
Inhibition of osteoblast differentiation	40	32.0
Inhibition of osteoclast differentiation	46	36.8
Interference with bone modeling	28	22.4
Staging includes		
2 stages	8	6.4
3 stages	39	31.2
4 stages	47	37.6
Not aware	31	24.8
Drug holiday concepts is and recommended drug holiday for is		
Drug is no longer available for consumption, 2 months	30	24.0
No idea	34	27.2
When patient stops taking a medication for a period of time, 10 years	13	10.4
When patient stops taking a medication for a period of time, 3–5 years	48	38.4
Duration of MRONJ to occur {minimum}		
3 weeks	27	21.6
5 weeks	23	18.4
More than 8 weeks	44	35.2
Not aware	31	24.8
Risk factors for MRONJ include		
All of the above	87	69.6
Dental implants	12	9.6
Patients with ongoing treatment for cancer or osteoporosis	17	13.6
Tooth extraction	9	7.2
Does MRONJ affect healing of extraction wound		
May be	44	35.2
No	12	9.6
Yes	69	55.2
Diagnosis by		

(Contd...)

**Table 2:** (Continued).

Descriptive Statistics: Responses		
Questionnaire	Frequency	Percent
Biopsy	22	17.6
Clinical evidence of necrotic bone	45	36.0
Non-healing extraction wound for >8 weeks	32	25.6
Radiographically	26	20.8
Treatment modalities are		
Can be managed surgically as well as conservatively	82	65.6
Conservative	6	4.8
Not aware	26	20.8
Surgical only	11	8.8
Surgical intervention is required in		
All the stages	33	26.4
Stage 2	16	12.8
Stage 2 and 3	48	38.4
Stage3	28	22.4
First line of choice of antibiotics include		
Clindamycin	16	12.8
Macrolides	11	8.8
Metronidazole	50	40.0
Penicillins	48	38.4

MRONJ: Medication-related osteonecrosis of jaws

**Table 3:** Designation based awareness about MRONJ.

Association between designation and responses			
Questionnaire	Designation		P-value
	Intern	Postgraduate	
Are you aware of medication-related osteonecrosis of jaws?			
Never heard	11.458333	0	0.004*
No	22.916667	3.4482759	
Yes	65.625	96.551724	
Which drugs can cause medication-related osteonecrosis?			
Anti angiogenic drugs	7.2916667	10.344828	0.279
Bisphosphonates	19.791667	24.137931	
Denosumab	11.458333	0	
All of the above	61.458333	65.517241	
Which jaw it affects more?			
Equal frequency in both	16.666667	6.8965517	0.000**
Mandible	57.291667	51.724138	
Maxilla	8.3333333	41.37931	
Not aware	17.708333	0	
Pathogenesis is related to			
Angiogenesis	10.416667	3.4482759	0.142
Inhibition of osteoblast differentiation	30.208333	37.931034	
Inhibition of osteoclast differentiation	33.333333	48.275862	
Interference with bone modeling	26.041667	10.344828	
Staging includes			
2 stages	7.2916667	3.4482759	0.000**
3 stages	31.25	31.034483	
4 stages	29.166667	65.517241	
Not aware	32.291667	0	

(Contd...)

**Table 3:** (Continued).

Questionnaire	Association between designation and responses		P-value
	Designation		
	Intern	Postgraduate	
Drug holiday concepts is and recommended drug holiday for is			
Drug is no longer available for consumption, 2 months	25	20.689655	0.010*
No idea	33.333333	6.8965517	
When patient stops taking a medication for a period of time, 10 years	10.416667	10.344828	
When patient stops taking a medication for a period of time, 3–5 years	31.25	62.068966	
Duration of MRONJ to occur {minimum}			
3 weeks	26.041667	6.8965517	0.000**
5 weeks	20.833333	10.344828	
More than 8 weeks	20.833333	82.758621	
Not aware	32.291667	0	
Risk factors for MRONJ include			
All of the above	61.458333	96.551724	0.004*
Dental implants	12.5	0	
Patients with ongoing treatment for cancer or osteoporosis	16.666667	3.4482759	
Tooth extraction	9.375	0	
Does MRONJ affect healing of extraction wound			
May be	45.833333	0	0.000**
No	11.458333	3.4482759	
Yes	42.708333	96.551724	
Diagnosis by			
Biopsy	20.833333	6.8965517	0.039*
Clinical evidence of necrotic bone	30.208333	55.172414	
Non-healing extraction wound for >8 weeks	25	27.586207	
Radiographically	23.958333	10.344828	
Treatment modalities are			
Can be managed surgically as well as conservatively	56.25	96.551724	0.002*
Conservative	6.25	0	
Not aware	27.083333	0	
Surgical only	10.416667	3.4482759	
Surgical intervention is required in			
All the stages	33.333333	3.4482759	0.000**
Stage 2	15.625	3.4482759	
Stage 2 and 3	27.083333	75.862069	
Stage 3	23.958333	17.241379	
First line of choice of antibiotics include			
Clindamycin	16.666667	0	0.013*
Macrolides	11.458333	0	
Metronidazole	35.416667	55.172414	
Penicillins	36.458333	44.827586	

MRONJ: Medication-related osteonecrosis of jaws, \*indicates P value is statistically significant

that they are prescribed and, hence, may fail to report them during dental examination. Therefore, it is mandatory for the clinician to take a thorough case history and do proper clinical examination for any procedure. This might help to prevent the condition.

The limitations of the study were that only small sample size was included and was conducted in a single institution. Much variation in the responses may not be recorded due to informal discussions among the respondents. The sample

size was unequal in both the groups, and hence, the results cannot be extrapolated to all dental professionals.

## CONCLUSION

The results imply that postgraduates were more aware about MRONJ as compared to interns. Although a higher level of awareness and knowledge was found in postgraduate group, not all of them were aware about the concept. Furthermore, in depth, understanding about the condition is very important

for prevention and treatment of the clinical condition as no effective treatment has been developed till date.<sup>[4]</sup> Thus, there is need for development of educational interventions and further research to reduce the risk of medication-related osteonecrosis for enhancement of patients health by dental professionals.

#### **Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent.

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Nil.

#### **Conflicts of interest**

There are no conflicts of interest.

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