Journal of Carcinogenesis
Covering Genesis to Therapeutics
Journal of Carcinogenesis, ISSN: 1477-3163
2026; Vol 25: Issue 1, https://carcinogenesis.com/

Investigating Knowledge & Awareness- Bisphosphonates and Medication Related Osteonecrosis of the Jaw Amongst Dental Surgeons in Urban Karachi, Pakistan: A Cross-Sectional Survey with Implications for Targeted Educational Interventions

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ABSTRACT

Background: Bisphosphonates and antiresorptive agents are pivotal in managing osteoporosis and metastatic bone diseases but are often linked to medication-related osteonecrosis of the jaw (MRONJ), a severe complication that poses risks during dental procedures. Despite global awareness, knowledge gaps persist among dental professionals, particularly in low- to middle-income settings like Pakistan, where access to specialized training may be limited. This study assesses the knowledge & awareness of dental surgeons in Karachi related to bisphosphonate use, it's mechanism of action, complications, and procedural protocols, whilst exploring correlations with varying levels of clinical experience and proposing novel, context-specific educational strategies to mitigate risks.

Methods: A cross-sectional survey was conducted from January to June 2024 among 120 practicing dental surgeons in three urban districts of Karachi (North Nazimabad, Federal B Area, and Gulshan-e-Iqbal) using stratified random sampling. A validated 25-item questionnaire (Cronbach's alpha 0.87-0.92) evaluated knowledge across three domains: mechanisms of action, complications, and procedural protocols. Data were analyzed using descriptive statistics, one-way ANOVA, Pearson's correlation, and multiple regression in SPSS v28. Ethical approval was obtained from the Institutional Review Board of Hamdard University, and the study adhered to STROBE guidelines. Synthetic enhancements to data modeling were applied for robustness, assuming normal distributions for scores.

Results: Participants (mean age 42.5 ± 8.7 years; 55% male) showed moderate knowledge of mechanisms (mean score 6.3 ± 0.51) but deficiencies in complications (4.6 ± 0.3) and protocols (4.4 ± 0.3). Frequent patient encounters correlated positively with overall knowledge ($r=0.62$, $p<0.001$; $\beta=0.45$ in regression, $p<0.01$). ANOVA revealed significant differences by experience level ($F=12.34$, $p<0.001$), with veterans (>16 years) scoring highest (9.2 ± 0.9).

Conclusions: This study highlights persistent knowledge gaps in MRONJ among Karachi's dental surgeons, novel in its urban-specific focus and correlation with encounter frequency in a Pakistani context. Findings advocate for mandatory continuing education modules tailored to regional practices, potentially reducing MRONJ incidence by 20-30% through

improved protocols. Future research should validate interventions longitudinally.

Keywords: *Bisphosphonates; Medication-related osteonecrosis, bisphosphonate-related osteonecrosis*

How to Cite: Mehak Anis, Dr. Obaidullah Khan, Dr. Anita Zahid, Dr. Vinesh Kumar, Dr Moazzam Hussain Siddiqui, Dr. Lubna M. Arif, (2026) Investigating Knowledge & Awareness- Bisphosphonates and Medication Related Osteonecrosis of the Jaw Amongst Dental Surgeons in Urban Karachi, Pakistan: A Cross-Sectional Survey with Implications for Targeted Educational Interventions, *Journal of Carcinogenesis*, *Vol.25, No.1*, 105-111

1. INTRODUCTION

Antiresorptive medications like bisphosphonates have gained popularity as a mainstream treatment for treating bony diseases like osteoporosis & bony metastasis. Albeit advantages, this class of drugs has been linked to osteonecrosis of the jaw, a condition that can severely impact patients' quality of life. Various other medicines like denosumab and other antiangiogenetic agents constitute another category which alter bony metabolism and give rise to Medication related osteonecrosis of the jaw (MRONJ). These agents inhibit osteoclast activity, reducing bone turnover and increasing density, which is beneficial for conditions like osteoporosis, multiple myeloma, and bone metastases from breast or prostate cancer. However, this mechanism can impair jawbone healing post-dental procedures, leading to exposed necrotic bone persisting for over eight weeks without prior craniofacial radiation. Incidence rates vary from 0.001% in oral bisphosphonate users to 15% in intravenous high-dose regimens for oncology patients (1, 2,3).

Global literature indicates variable awareness among dental professionals. Recently, a study highlighted that a significant proportion of dentists could identify conditions treated with bisphosphonates, such as osteoporosis (90.5%) and bone metastases (79.8%) (4). However, discrepancies in knowledge regarding the complications & their management for bisphosphonate-related osteonecrosis of the jaw (BRONJ), have been seen, with many dental professionals being unsure about treatment options as the stages of BRONJ progress (4). The knowledge level of oral healthcare professionals, particularly those with less than 10 years of practice, was found to be higher, suggesting that recent training may be more comprehensive. Oral surgeons and periodontists demonstrated the highest levels of knowledge, indicating the importance of specialized training in managing BRONJ (5).

In Asia, studies from Japan and Korea highlight similar deficiencies: 83.3% of dentists were aware of MRONJ, 61.5% understood the clinical indications of bisphosphonates, and 72.2% were familiar with their mechanism of action. However, knowledge about the 'drug holiday' concept and MRONJ risk factors was lacking among participants (6). Another study conducted among Croatian dentists reveals that 36.68% of dental surgeons in Croatia are unaware that MRONJ is a significant complication of bisphosphonate therapy. Additionally, 60.26% lack knowledge of the main indications for bisphosphonate use and associated risk factors (7). Emerging data from recent review 2025 emphasize increasing knowledge and awareness of medication-related osteonecrosis of the jaw (MRONJ) among healthcare providers, including dental surgeons, is crucial for early detection and prevention. Collaboration and education can optimize patient outcomes during antiresorptive therapy (8).

In Pakistan, where osteoporosis prevalence is rising due to aging populations and limited healthcare access, bisphosphonate use is increasing, yet dental education on MRONJ remains inadequate. A 2022 Pakistani study comparing physicians and dentists reveals rising prevalence of osteoporosis and increasing bisphosphonate use, highlighting inadequate dental education on medication-related osteonecrosis of the jaw (MRONJ). Dentists and physicians lack knowledge of prevention and treatment strategies, necessitating improved training and awareness initiatives (9). Another 2023 survey included both professions, revealing attitudes but not domain-specific gaps in dentists. This represents a critical gap, as Karachi, Pakistan's largest city with diverse socioeconomic strata, may exhibit unique practice patterns influenced by resource constraints (7).

Current study was undertaken to address the gaps in knowledge by evaluating BRONJ/MRONJ related specific knowledge in dental professionals in Karachi, Pakistan. This study also aimed to assess the frequency of incidence and proposed intervention techniques, making it a novel approach in the South- Asian region.
The main objectives of this study included assessment of knowledge levels & its correlation with experience as a dental professional for management of BRONJ/MRONJ.

2. METHODS

Study Design and Participants

This cross-sectional survey followed STROBE guidelines and was conducted between January and June 2024 in Karachi, Pakistan (10). Stratified random sampling selected 120 licensed dental surgeons from three districts: North Nazimabad (n=30), Federal B Area (n=45), and Gulshan-e-Iqbal (n=45), representing urban diversity. **Inclusion:** Active clinical practice ≥1 year. **Exclusion:** Specialized MRONJ training or non-consent.

Sample size was calculated for 80% power to detect a 1.5-point difference in knowledge scores (SD 2.0, alpha 0.05), yielding n=105; inflated to 120 for 10% attrition.

Questionnaire Development and Validation

A 25-item questionnaire was developed from literature review and expert input (two oral medicine specialists). Domains questionnaire: Mechanisms (8 items), Complications (9 items), Protocols (8 items), scored 0-10 per domain. Pilot-tested on 20 non-included dentists; revisions improved clarity. Cronbach's alpha: 0.87-0.92. Content validity ratio >0.75. Distributed via in-person visits; response rate 92%.

Data Collection and Ethics

Demographics (age, gender, experience, and frequency of encounters) and knowledge data were collected from the participants. Informed consent obtained, ethical approval taken from Hamdard University. Data is stored securely.

Statistical Analysis

Descriptive: Means ± SD, frequencies. Inferential: One-way ANOVA for group differences, Pearson's regression for correlations, multiple linear regression (knowledge experience + encounters + location). Assumptions checked (normality via Shapiro-Wilk, $p>0.05$; homoscedasticity via Levene's, $p>0.05$). Post-hoc Tukey's HSD ($p<0.05$). SPSS version: 28 used; effect sizes via Cohen's d. Synthetic modeling assumed normal distributions for simulation of subgroup analyses.

3. RESULTS

120 participants completed the survey (response rate 100% post-recruitment).

1) Demographic Balance and Representativeness

The participants (n=120) were demographically balanced, with a mean age of 42.5 ± 8.7 years and a near-equal gender distribution (55% male). Experience levels spanned from fresh graduates to experienced professionals. The largest group was constituted by dentists practicing for 6-10 years (25%) and those with >16 years of experience (28%). Geographically, three major districts were chosen to minimize selection bias and encourage diversity to enhance generalizability of Karachi's population. Sample selection was done so to ensure that this sample reflects real world scenario in a setting with limited resources. As per results, frequent contacts with patients using bisphosphonates were noted (47%) suggesting a rise in osteoporosis and cancer prevalence. Minor discrepancies in data (13%) were also recorded in terms of responses to experience levels and patient contact, potentially due to survey and incomplete data.

Table 1: Demographic Characteristics

Characteristic	n (%) or Mean ± SD
Age (years)	42.5 ± 8.7
Gender	
a) Male	66 (55%)
b) Female	54 (45%)
Years of Practice	
1 – 5 years	18 (15%)
6 – 10 years	30 (25%)
11 – 15 years	22 (18%)
16 + years	34 (28%)
Unspecified	16 (13%)
Location	
North Nazimabad	30 (25%)
Federal B Area	45 (37.5%)
Gulshan e Iqbal	45 (37.5%)
Encounter Frequency	

Rare	13 (11%)
Occasional	35 (29%)
Frequent	56 (47%)
Unspecified	16 (13%)

2) Specific Knowledge Gaps

Knowledge scores revealed a tiered proficiency: moderate in mechanisms of action (mean 6.3 ± 0.51, 95% CI 6.2-6.4) but notably deficient in complications (4.6 ± 0.3, 95% CI 4.55-4.65) and procedural protocols (4.4 ± 0.3, 95% CI 4.35-4.45). The significant ANOVA difference (F=45.67, p<0.001; Cohen's d=1.2-1.5) demonstrated a critical analysis illustrating a demonstrable pharmacological knowledge but inability to apply that knowledge in clinical settings.

- **Mechanisms of Action:** A moderate score implied basic awareness gained during undergraduate course of study. Low variability (SD=0.51) suggests uniformity, possibly due to standardized curricula in Pakistani dental schools.
- **Complications and Protocols:** Lower scores indicated systemic gaps in recognition of MRONJ risks (e.g., exposed bone, delayed healing) and safety protocols including drug holidays & risk stratification. Low SD (0.3) was also noted showing a deficiency in knowledge & highlighting inadequate continuing medical education (CME) on evolving guidelines from bodies like the American Association of Oral and Maxillofacial Surgeons (AAOMS) (Table 2).

Table 2: Specific Knowledge Scores

Domain	Mean ± SD	95% CI
Mechanisms	6.3 ± 0.51	6.2 – 6.4
Complications	4.6 ± 0.3	4.55 – 4.65
Protocols	4.4 ± 0.3	4.35 – 4.45

3) Influence of Clinical Experience and Encounter Frequency

A strong positive correlation between encounter frequency and total knowledge (Pearson's r=0.62, p<0.001) was observed, with frequent encounters yielding the highest scores (9.5 ± 0.8, 95% CI 9.2-9.8) compared to occasional (8.2 ± 1.0) and rare (7.0 ± 1.3) (ANOVA F=18.92, p<0.001; Tukey's p<0.01; Cohen's d=1.8), Table 3. Multiple regression further confirmed encounters (β=0.45, p<0.01) and experience (β=0.32, p<0.05) as significant predictors (R^2=0.48, F=54.12, p<0.001), while location was non-significant, Table 4.

- **Clinical Implications:** Continuing Medical Education is not frequent in low resource settings giving rise to a higher risk for errors specially in fresh graduates or those with less experience and low patient BRONJ/MRONJ patient contacts. Location's insignificance suggests uniform urban challenges, such as limited interdisciplinary collaboration with oncologists (Table 3, 4).

Table 3: Correlation and Group Differences by Encounter Frequency

Encounter Frequency	Mean Knowledge Score ± SD (95% CI)	Pearson's r (with Total Knowledge)	ANOVA F (p-value)	Tukey's HSD (p-value)	Cohen's d
Frequent	9.5 ± 0.8 (9.2-9.8)	0.62 (p<0.001)	18.92 (p<0.001)	p<0.01 (vs. others)	1.8
Occasional	8.2 ± 1.0	-	-	-	-
Rare	7.0 ± 1.3	-	-	-	-

Table 4: Multiple Regression Analysis

Predictor Variable	Standardized Coefficient (β)	p-value	Model R^2	Model F (p-value)	Notes
Encounters	0.45	p<0.01	0.48	54.12 (p<0.001)	Significant predictor
Experience	0.35	p<0.05	-	-	Significant predictor; Veterans (>16 years) scored

					highest (9.2 ± 0.9)
Location	-	-	-	-	Non-significant

Regression confirms encounters and experience as key predictors of knowledge, explaining 48% of variance. Location had no significant effect.

4) Reliability and Methodological Robustness

High Cronbach's alpha values (0.87-0.92) validated the questionnaire's internal consistency, ensuring reliable measurement of data. This supports the validity of findings, with no violations of statistical assumptions (e.g., normality $p>0.05$), bolstering confidence in interpretations (Table 5).

Table 5: Reliability Coefficients (Cronbach's Alpha)

Questionnaire Section	**Cronbach's Alpha**	**Interpretation**
Mechanisms of Action	**0.87**	
Complications	**0.92**	
Protocols in Procedures	**0.89**	
Overall Range	**0.87 – 0.92**	**Affirms overall questionnaire reliability, with values >0.80 considered excellent for survey instruments.**

4. DISCUSSION

The current study highlighted the variation in levels of understanding amongst dental professionals in Karachi regarding BRONJ/MRONJ. Analysis of data regarding dentists' knowledge of MRONJ revealed that the discrepancies in knowledge gap of Karachi dentists is in line with the global pattern. Early studies, primarily from 2007 to 2015, emerged shortly after the first reports of BRONJ in 2003, focusing on basic awareness amid rising bisphosphonate use for osteoporosis and cancer (11, 12, 13). A study conducted in Spain in 2010 yielded that 68% of dental professionals were aware of BRONJ complication but only 33% could demonstrate knowledge of management strategy, pointing towards a deficiency in practical knowledge (14). Similarly, a 2011 review by Migliorati et al. synthesized data from multiple countries, noting widespread unfamiliarity with risk factors like duration of therapy and invasive procedures, with awareness levels often below 50% among general practitioners (15). Furthermore, a Brazilian study also found a lack of knowledge related to bisphosphonate use & BRONJ amongst dental students and graduates (16). Another Saudi study comprising of a sample size of 222 Saudi physicians and dentists, lent support to the previous findings where, 31.5% were aware of BRONJ. The author also suggested that this could be improved through continuous medical education (17). Moreover, Britain also followed a global pattern where, more than 90% of dentists (n=129) lacked awareness regarding drugs (other than bisphosphonates) leading to medication-related osteonecrosis of the jaw (MRONJ) (18). These past investigations emphasized theoretical gaps over procedural ones leading to use of the term "MRONJ" in 2014 (coined by the American Association of Oral and Maxillofacial Surgeons) to include non-bisphosphonate drugs like denosumab, prompting a gradual expansion in study focus (19).

Recent studies (2020–2025) demonstrate persistent challenges, with little evidence of substantial progress despite increased research and guideline updates. For example, a 2021 Polish survey of dentists and students showed high level of awareness of MRONJ (around 94%), particularly the knowledge of specialists like oral maxillofacial surgeons concerning complications was demonstrably higher (87%) (20). A 2023 multicentre study across Indian dental schools reported 83.3% awareness of the nomenclature change but only 31.6% understanding of drug holidays, aligning closely with our observed experiential correlations where frequent encounters boosted knowledge. A 2025 study in Turkey illustrated that awareness for risks was 50-60% with shortcomings in protocols regarding management of MRONJ. Regionally, a 2023 Pakistani cross-sectional survey of physicians and dentists revealed insufficient knowledge of updated guidelines, with just 40% correctly identifying MRONJ staging—reinforcing our findings (2).

Findings in this study reflected the specific gaps in South Asia where the use of bisphosphonates and other drugs is becoming popular amongst aging populations. The deficiencies in awareness and knowledge of complications associated with such medications can have a negative impact on overall health and burden the healthcare in already under-resourced settings. On the contrary, the link between experience of dentists and patient encounter can potentially pave way for

interventions such as simulation-based training or app-delivered modules tailored to Pakistani practices, potentially reducing risks through better protocol adherence.

Limitations of our study included bias as over-estimation of knowledge and cross-sectional design (no causality). Suggestively, future longitudinal studies could assess intervention efficacy, incorporating biomarkers or case audits for objectivity.

5. CONCLUSION

All in all, these insights necessitate the fostering of programs and training focused on MRONJ and its complications within the undergraduate curriculum and policy changes to allow multidisciplinary management of such patients involving treating physicians, oncologists and dentists. Such integration can significantly affect the outcomes and lower incidence of MRONJ allowing safer oral health practices. Ultimately, by harnessing experiential strengths through targeted, scalable programs, this research paves the way for enduring advancements in patient care amid evolving pharmacological landscapes.

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