



Expert Perspectives on the Clinical Experience of Managing Osteoporosis and Osteoarthritis in Indian Settings

Manjula S^{a++*} and Krishna Kumar M^{a#}

^a Department of Medical Services, Micro Labs Limited, Bangalore, Karnataka, India.

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/125154>

Original Research Article

Received: 18/08/2024

Accepted: 20/10/2024

Published: 28/10/2024

ABSTRACT

Objective: This study aimed to gather expert opinions on the clinical experience and management of osteoporosis (OP) and osteoarthritis (OA) in Indian settings.

Methodology: The cross-sectional study utilized CORE-2, a multi-response questionnaire booklet comprising 24 questions to gather insights from experts across various regions of India. The survey included questions regarding prevalence, risk factors, screening methods, prevention, and the benefits of calcitriol, paracetamol, and tramadol for managing OP and OA symptoms. Descriptive statistics were employed to analyze the collected data.

Results: Out of 142 survey participants, the majority (71%) identified excessive alcohol consumption, family history, smoking, poor diet, older age, and post-menopausal status as common risk factors for OP. Nearly half (42.96%) of the experts indicated that blood tests, dual-energy X-ray absorptiometry (DEXA) scans, bone turnover markers, and bone mineral density (BMD) ultrasound

⁺⁺ Sr. Vice President;

[#] Sr. General Manager;

^{*}Corresponding author: Email: drmanjulas@gmail.com;

Cite as: S, Manjula, and Krishna Kumar M. 2024. "Expert Perspectives on the Clinical Experience of Managing Osteoporosis and Osteoarthritis in Indian Settings". *Asian Journal of Orthopaedic Research* 7 (2):100-108. <https://journalajorr.com/index.php/AJORR/article/view/195>.

are the most commonly utilized screening methods for OP. Around 46% of clinicians acknowledged that elevated body weight increases the risk of osteoporotic fractures. The majority (76.06%) agreed that calcitriol assists in managing fractures, with weekly dosages enhancing patient compliance and treatment efficacy in OP management. According to 63% of the experts, excess body weight was linked to an increased likelihood of OA. Approximately 58% recognized that glucocorticoid-induced osteoporosis (GIOP) can predispose individuals to fractures and falls. Nearly 68% of clinicians favoured non-steroidal anti-inflammatory drugs (NSAIDs), physiotherapy, diet, and exercise as initial management approaches for OA.

Conclusion: This study highlighted the roles of excessive alcohol consumption, family history, and obesity in both OA and OP. The preferred screening methods include DEXA scans and BMD ultrasounds, and calcitriol was recognized for its effectiveness in managing fractures. Furthermore, there was a consensus on the importance of lifestyle interventions, including diet, exercise, and the use of non-steroidal anti-inflammatory drugs in OA management.

Keywords: Fractures; vitamin D; calcitriol; calcium; paracetamol; analgesic effect.

1. INTRODUCTION

Osteoporosis (OP) and osteoarthritis (OA) are distinct musculoskeletal conditions with significant impacts on global health [1,2]. As of 2019, there were 41.5 million reported cases of OP globally, a number projected to rise to 263.2 million by 2030-2034, accompanied by an anticipated burden of 128.7 million disability-adjusted life years (DALYs). Similarly, OA affected approximately 595 million people worldwide in 2020, marking a substantial 132.2% increase since 1990. Projections indicate a significant rise in knee, hand, hip, and other forms of OA by 2050 compared to 2020 levels [3,4].

In India, the estimated prevalence of OP in women ranges from 8% to 62%, primarily driven by factors such as inadequate dietary calcium, vitamin D deficiency, and changing lifestyles. Concurrently, the number of individuals affected by OA rose from around 23.46 million in 1990 to 62.35 million by 2019. This increase in prevalence is linked to rising age-standardized prevalence rates and DALYs, underscoring the escalating public health challenge posed by these musculoskeletal disorders in the country [5].

Calcitriol, the active biological form of vitamin D, operates as a traditional hormone in preserving skeletal health through the regulation of calcium and phosphorus metabolism. It enhances intestinal absorption of calcium and phosphate, promotes bone mineralization, and regulates parathyroid hormone levels. In clinical practice, calcitriol is often prescribed for conditions like OP, chronic kidney disease, and hypoparathyroidism to prevent or treat bone-

related disorders. Its benefits include improving bone density, reducing the risk of fractures, and supporting overall bone health. Additionally, calcitriol may have immunomodulatory effects, influencing the immune response in various conditions [6,7].

Paracetamol, a non-steroidal anti-inflammatory drug (NSAID), primarily exerts its analgesic effect by activating serotonin-mediated descending pathways centrally. Paracetamol primarily acts by inhibiting cyclooxygenase (COX) enzymes in the central nervous system, reducing the synthesis of prostaglandins involved in pain and fever. It may also activate descending serotonergic pathways and interact with the endocannabinoid system to enhance its analgesic effects. In OA, paracetamol is often recommended as a first-line treatment due to its safety profile and lower risk of gastrointestinal side effects compared to non-steroidal anti-inflammatory drugs. In OP, paracetamol is used primarily to manage pain resulting from fractures or other complications related to the disease [8].

Tramadol, an opioid analgesic, is used to manage moderate to severe pain in patients with OA and OS. It selectively binds to multiple opioid receptors binding to μ -opioid receptors, inhibiting the reuptake of serotonin and norepinephrine, which enhances its analgesic effects. This dual mechanism helps in modulating pain perception and response [9]. The survey aims to collect expert opinions on managing OP and OA in Indian clinical settings to guide standardized treatment practices, highlight effective screening methods, and inform targeted prevention and early management strategies for better patient outcomes.

2. MATERIALS AND METHODS

We carried out a cross-sectional, multiple-response questionnaire-based study involving clinicians with expertise in managing osteoporosis (OP) and osteoarthritis (OA) in major Indian cities from June 2023 to December 2023.

2.1 Questionnaire

The questionnaire booklet named CORE-2 (Comprehensive Osteoporosis & Osteoarthritis Evaluation) study was sent to the clinicians who were interested in participating in this study. The CORE-2 study questionnaire consisted of 24 questions focused on current prescription practices, clinical observations, and experiences with OP and OA in routine practice. The study was conducted after getting approval from Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian Regulatory Authority, Drug Controller General of India.

2.2 Participants

An invitation was sent to leading clinicians in treating OP and OA in the month of March 2023 for participation in this Indian survey. About 142 doctors from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provided necessary data. Participants were asked to complete the questionnaire without discussing it with their peers.

2.3 Statistical Methods

Convenient sampling method was used in this study. Descriptive statistics were conducted for data analysis. Categorical variables were represented as percentages to depict their distribution. The frequency of each variable's occurrence and the corresponding percentage were used to visualize their distribution through bar charts, created using Microsoft Excel 2013 (version 16.0.13901.20400).

3. RESULTS

Among 142 surveyed clinicians, over half (53.52%) of them reported that 21-30% of women presenting to routine settings have OP. Additionally, 44% of respondents indicated that

11-20% of women over 50 years of age experience bone fractures. About 38% of participants noted that 11-25% of OP patients experience exercise-related fractures. According to 41% of clinicians, men over 50 years of age have a higher rate of bone loss compared to women. A significant majority (71%) recognized excessive alcohol consumption, family history, smoking, poor diet, older age, and post-menopausal status as common risk factors for OP (Fig. 1). Nearly half (42.96%) of respondents stated that blood tests, dual-energy x-ray absorptiometry (DEXA) scans, bone turnover markers, and bone mineral density (BMD) ultrasound are the most used screening methods for OP (Table 1).

Table 1. Distribution of response to most frequently used screening methods for OP in routine settings

Test	Response rate (n = 142)
Blood test	0.7%
DEXA scan	20.42%
Bone turnover marker (BTM) measurements	7.75%
BMD by ultrasound	28.17%
All of the above	42.96%

Around 30% of the clinicians reported that full blood count tests are not useful for evaluating secondary causes of OP. About 40% of the respondents stated that 21-30% of OP patients suffer from vertebral compression fractures. Approximately 46% indicated that increased body weight enhances the risk of osteoporotic fractures (Fig. 2). According to 38% of the participants, bone mineral accretion is notably high after menopause in women. The majority (76.06%) of the clinicians agreed that calcitriol aids in fracture management, with weekly dosages improving patient compliance and effectiveness in managing OP (Table 2).

More than half (53.52%) of the clinicians reported that 21-30% of the patients with OA present in routine settings. About 53% of respondents stated that they diagnose OA most frequently in the 40–49-year age group. Around 39% noted that 21-40% of obese patients have OA. Additionally, 63% of the clinicians attributed excess body weight to an increased likelihood of developing OA (Fig. 3).

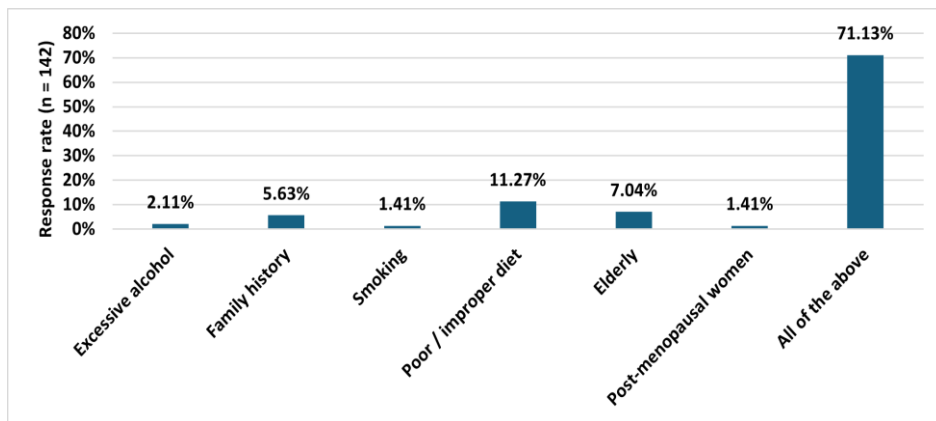


Fig. 1. Distribution of response to common risk factors for OP noted among subjects presenting to routine practice

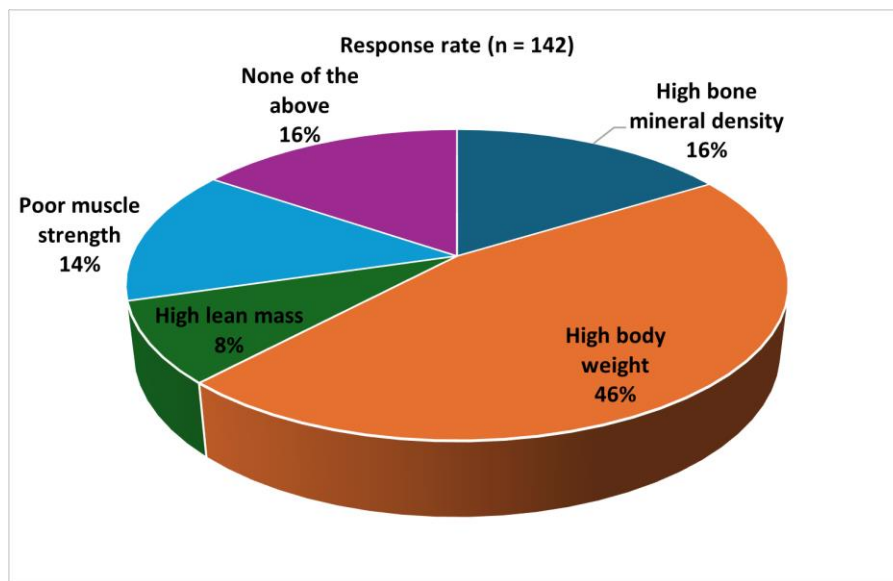


Fig. 2. Distribution of response to factors increasing the risk of OP fracture

Table 2. Distribution of response to preferred choice between calcitriol and vitamin D3

Opinion	Response rate (n = 142)
Calcitriol helps in fracture management	5.63%
The weekly dosage makes it patient-compliant	10.56%
Effective in OP management	7.75%
All of the Above	76.06%

About 36% of the experts observed that 11-20% of OA patients also have OP. Most of the clinicians (71.83%) noted that the knee is the most affected joint in OA cases. Approximately 42% of the respondents reported that osteopenia is a characteristic of OA joints compared to aging joints. According to 57% of clinicians, overweight or obesity is the significant modifiable risk factor for severe knee OA. Moreover, 75% pointed out

the knee joint as the most affected joint among men. Approximately 58% of the experts acknowledged that glucocorticoid-induced OP (GIOP) can lead to fractures and falls (Table 3).

Almost 68% of the experts preferred NSAIDs, physiotherapy, diet, and exercise as initial management strategies for OA (Fig. 4). According to 32% of the clinicians, 11-20% of

newly diagnosed OA patients would require joint replacement surgery. About 42% highlighted paracetamol and tramadol for their faster onset and longer duration in managing OA (Table 4).

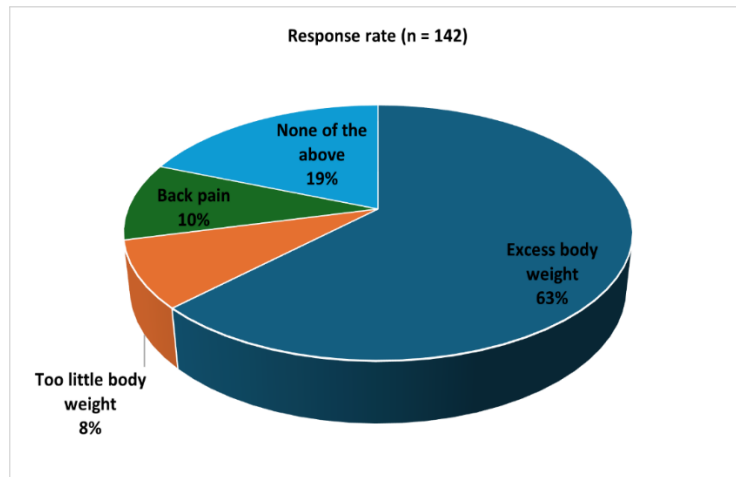


Fig. 3. Distribution of response to opinion on factors increasing the likelihood of OA

Table 3. Distribution of response to importance of preventing and treating glucocorticoid-induced OP

Importance	Response rate (n = 142)
GIOP is associated with other chronic diseases	21.83%
GIOP can lead to fracture and falls	57.75%
Myopathy	11.97%
No impact	8.45%

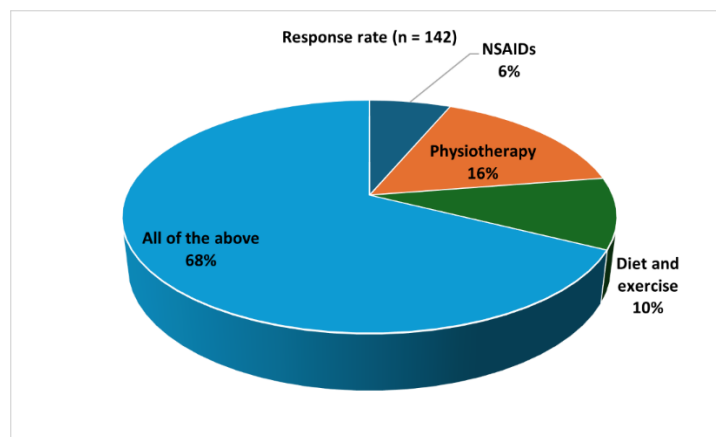


Fig. 4. Distribution of response to preference on early management strategies for OA

Table 4. Distribution of response to opinion on the use of paracetamol and tramadol in OA management

Opinion	Response rate (n = 142)
Effective in short-term and long-term pain management	23.24%
Effective in reducing chronic low back pain	20.42%
Faster onset and longer duration of action	41.55%
Tolerable in respiratory distress	14.79%

4. DISCUSSION

The present survey represents a comprehensive exploration of OP and OA, examining various facets such as diagnosis, symptom management, and treatment methods based on a cross-sectional survey of clinicians. According to the findings, Vitamin D3, paracetamol, and tramadol are highly effective medications for managing both conditions. Most of the survey respondents highlighted common risk factors for OP including excessive alcohol consumption, family history, smoking, poor diet, older age, and post-menopausal status. Ibrahim et al. underscored factors like low body mass index (BMI), vitamin D deficiency, inadequate calcium intake, excessive caffeine and alcohol consumption, smoking, sedentary lifestyle, lack of physical activity, endocrine disorders, certain medications, and history of fragility fractures as associated with OP risk. Non-modifiable risk factors identified were being female gender, having a family history, belonging to a specific race, and experiencing early menopause [10].

Zhang et al. found a nonlinear relationship between alcohol consumption and hip fracture risk, with moderate intake inversely linked to risk and heavy consumption associated with increased risk [11]. Ortego-Centeno et al. noted that smoking contributes to reduced bone mass and higher osteoporotic fracture risk [12]. Zou et al. identified age, female gender, early menopause, smoking, alcohol consumption, inadequate vitamin D intake, systemic inflammatory response, low BMI, and corticosteroid use as shared risk factors for both OP and chronic obstructive pulmonary disease (COPD) [13]. Lane reported various risk factors for OP fractures, including low peak bone mass, hormonal influences, glucocorticoid use, smoking, physical inactivity, inadequate calcium and vitamin D intake, ethnicity, small body size, and personal or family history of fractures [14].

About half of the respondents identified BMD ultrasound, DEXA scans, bone turnover markers, and blood tests as commonly used screening methods for OP. According to de Oliveira et al., DEXA and the fracture risk assessment tool are the most frequently utilized methods in this regard [15]. Kling et al. further emphasized that DEXA is the primary validated technique for measuring BMD and diagnosing OP [16]. The United States Preventive Services Task Force (USPSTF) recommends bone measurement testing for screening women aged 65 and older

to prevent osteoporotic fractures [17]. Njeh et al. found that combining ultrasound and DEXA BMD results significantly improve the prediction of hip fractures [18].

Most of the survey respondents indicated that elevated body weight increases the risk of osteoporotic fractures. Compston et al. highlighted that height and obesity have also been linked to higher fracture risk at certain locations [19]. Palermo et al. suggested that obesity, including fat mass, could potentially be a risk factor contributing to reduced bone density and increased fracture risk [20].

Most of the respondents agreed that calcitriol aids in fracture management, with weekly dosages improving patient compliance and effectiveness in managing OP. Aloia et al. reported that calcitriol increases bone mineral density (BMD) by reducing bone resorption [21]. Peppone et al. recommended considering calcitriol, either alone or in combination with other agents, for the treatment of OP [22].

Most respondents indicated that excess body weight significantly increases the risk of OA. Nedunchezhiyan et al. emphasized that increased body weight leads to excessive joint loading, contributing to OA by causing articular cartilage deterioration [23]. King et al. underscored that obesity is the primary modifiable risk factor for OA [24], while Raud et al. identified obesity as a key risk factor for knee OA [25].

The survey respondents also acknowledged that GIOP can lead to fractures. Hayes et al. indicated that untreated GIOP can result in fractures in as many as 40% of patients undergoing chronic glucocorticoid therapy [26]. Similarly, Fraser and Adachi stated that GIOP is a significant consequence of glucocorticoid therapy, with fractures occurring in 30–50% of patients [27].

Many of the survey respondents preferred NSAIDs, physiotherapy, diet, and exercise as initial management strategies for OA. Lee et al. noted that many international guidelines recommend topical NSAIDs as an initial treatment option for managing OA pain [28]. Osthoff et al. and Kolasinski et al. emphasized that physical therapy is frequently advocated as the primary nonpharmacological and nonsurgical approach for managing musculoskeletal conditions, particularly OA [29,30]. Mackay et al.

highlighted that joint-specific exercises are an evidence-based strategy for managing OA [31]. Maly et al. noted that while diet alone can enhance physical function, combining it with exercise is essential to improve pain management [32].

Most of the current survey participants highlighted the use of paracetamol and tramadol for their faster onset and longer duration in managing OA. Gaul and Eschaliere found that higher doses of paracetamol provided significantly better pain relief ($P < 0.05$), faster onset of relief, and longer duration of pain relief compared to doses of 500 mg or 650 mg [33]. Dhillon reported that fixed-dose tramadol/paracetamol offers rapid onset, extended duration, and multifaceted pain relief, proving effective and generally well tolerated in patients experiencing moderate to severe pain [34]. Rawal et al. highlighted that the fixed-combination tablet containing tramadol HCL 37.5 mg/paracetamol 325 mg combines two components with distinct mechanisms of action. Tramadol HCL, a centrally acting weak opioid agonist and monoamine neurotransmitter reuptake inhibitor, has demonstrated efficacy in providing sustained relief for moderate to severe postoperative pain across various surgical procedures. While, paracetamol, known for its rapid onset of action, serves as a nonopioid analgesic and antipyretic, typically used for managing mild to moderate pain [35].

The survey findings underscore the necessity for personalized treatment strategies to improve patient outcomes and optimize care in OP and OA. The strengths of the study include a larger sample size and insights from practitioners specialized in OA and OP. However, reliance on expert opinion may have introduced potential bias, limiting the generalization of the survey findings. Therefore, further research and studies are warranted to validate these findings and enhance the understanding of effective management strategies for OP and OA.

5. CONCLUSION

The survey highlights the importance of recognizing common risk factors for OP and OA, such as excessive alcohol consumption, family history, and menopausal status. It identifies effective screening methods, including DEXA scans and ultrasound, and underscores the role of calcitriol in fracture management. Clinicians prioritize lifestyle modifications and initial

treatments like NSAIDs, physiotherapy, and the use of paracetamol and tramadol for pain relief. These findings emphasize the need for personalized treatment strategies to optimize care for patients with OP and OA.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

CONSENT

A written informed consent was obtained from each physician before initiation of the study.

ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGEMENT

We would like to thank all the experts who were participated in this study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Porter JL, Varacallo M. Osteoporosis. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024 [Accessed On:2024 Jul 29]. Available: <http://www.ncbi.nlm.nih.gov/books/NBK441901/>
2. Allen KD, Thoma LM, Golightly YM. Epidemiology of osteoarthritis. *Osteoarthritis and Cartilage*. 2022;30(2): 184–95.
3. Zhu Z, Yu P, Wu Y, Wu Y, Tan Z, Ling J. Sex Specific global burden of osteoporosis in 204 countries and territories, from 1990 to 2030: An Age-period-cohort modeling study. *The Journal of Nutrition, Health and Aging*. 2023;27(9):767–74.
4. GBD 2021 Rheumatoid arthritis collaborators. Global, regional, and national burden of rheumatoid arthritis, 1990-2020, and projections to 2050: A systematic analysis of the Global Burden

- of Disease Study 2021. *Lancet Rheumatol.* 2023;5(10):e594-e610.
5. Agrawal AC, Garg AK. Epidemiology of Osteoporosis. *Joio.* 2023;57(1):45–8.
 6. Calcitriol - An overview | ScienceDirect Topics. [Accessed On: 2024 Jul 29]. Available: <https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/calcitriol>
 7. Lung BE, Mowery ML, Komatsu DEE. Calcitriol. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2024 [Accessed On: 2024 Jul 29]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK526025/>
 8. Anderson BJ. Paracetamol (Acetaminophen): mechanisms of action. *Paediatr Anaesth.* 2008;18(10):915–21.
 9. Dhesi M, Maldonado KA, Patel P, Maani CV. Tramadol. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2024 [Accessed On: 2024 Jul 29]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK537060/>
 10. Ibrahim NA, Nabil N, Ghaleb S. Pathophysiology of the risk factors associated with osteoporosis and their correlation to the T-score value in patients with osteopenia and osteoporosis in the United Arab Emirates. *J Pharm Bioallied Sci.* 2019;11(4):364–72.
 11. Zhang X, Yu Z, Yu M, Qu X. Alcohol consumption and hip fracture risk. *Osteoporos Int.* 2015;26(2):531–42.
 12. Ortego-Centeno N, Muñoz-Torres M, Jódar E, Hernández-Quero J, Jurado-Duce A, de la Higuera Torres-Puchol J. Effect of tobacco consumption on bone mineral density in healthy young males. *Calcif Tissue Int.* 1997;60(6):496–500.
 13. Zou X, Ma Z, Liu X, Zhang K, Qiu C, Liang R, et al. Risk factors and prognostic value of osteoporosis in hospitalized patients with bronchiectasis. *BMC Pulm Med.* 2023;23(1):55.
 14. Lane NE. Epidemiology, etiology, and diagnosis of osteoporosis. *American Journal of Obstetrics & Gynecology.* 2006;194(2):S3–11.
 15. Oliveira MA de, Moraes R, Castanha EB, Prevedello AS, Vieira Filho J, Bussolaro FA,. Osteoporosis screening: Applied methods and technological trends. *Medical Engineering & Physics.* 2022;108:103887.
 16. Kling JM, Clarke BL, Sandhu NP. Osteoporosis prevention, screening, and treatment: A review. *J Womens Health (Larchmt).* 2014;23(7):563-72.
 17. US preventive services task force. screening for osteoporosis to prevent fractures: US preventive services task force recommendation statement. *JAMA.* 2018;319(24):2521–31.
 18. Njeh CF, Boivin CM, Langton CM. The role of ultrasound in the assessment of osteoporosis: A review. *Osteoporos Int.* 1997;7(1):7–22.
 19. Piñar-Gutierrez A, García-Fontana C, García-Fontana B, Muñoz-Torres M. Obesity and bone health: A complex relationship. *Int J Mol Sci.* 2022;23(15):8303.
 20. Palermo A, Tuccinardi D, Defeudis G, Watanabe M, D'Onofrio L, Lauria Pantano A. BMI and BMD: The potential interplay between obesity and bone fragility. *Int J Environ Res Public Health.* 2016;13(6):544.
 21. Aloia JF, Vaswani A, Yeh JK, Ellis K, Yasumura S, Cohn SH. Calcitriol in the treatment of postmenopausal osteoporosis. *The American Journal of Medicine.* 1988;84(3, Part 1):401–8.
 22. Peppone LJ, Hebl S, Purnell JQ, Reid ME, Rosier RN, Mustian KM. The efficacy of calcitriol therapy in the management of bone loss and fractures: a qualitative review. *Osteoporos Int.* 2010;21(7):1133–49.
 23. Nedunchezhiyan U, Varughese I, Sun AR, Wu X, Crawford R, Prasadam I. Obesity, inflammation, and immune system in osteoarthritis. *Front Immunol.* 2022;13:907750.
 24. King LK, March L, Anandacoomarasamy A. Obesity & osteoarthritis. *Indian J Med Res.* 2013;138(2):185-93.
 25. Raud B, Gay C, Guiguet-Auclair C, Bonnin A, Gerbaud L, Pereira B. Level of obesity is directly associated with the clinical and functional consequences of knee osteoarthritis. *Sci Rep.* 2020;10(1):3601.
 26. Hayes KN, Baschant U, Hauser B, Burden AM, Winter EM. When to start and stop bone-protecting medication for preventing glucocorticoid-induced osteoporosis. *Front Endocrinol (Lausanne).* 2021;12:782118.
 27. Fraser LA, Adachi JD. Glucocorticoid-induced osteoporosis: treatment update and review. *Ther Adv Musculoskelet Dis.* 2009;1(2):71-85.

28. Lee JK, Abbas AA, Cheah TE, Simanjuntak RN, Sockalingam S, Roohi S. Topical nonsteroidal anti-inflammatory drugs for management of osteoarthritis pain: A consensus recommendation. *Journal of Orthopaedic Research*. 2023;41(9):1916–24.
29. Rausch Osthoff AK, Niedermann K, Braun J, Adams J, Brodin N, Dagfinrud H. EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. *Ann Rheum Dis*. 2018;77(9):1251–60.
30. Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J. American college of rheumatology/arthritis foundation guideline for the management of osteoarthritis of the hand, Hip, and Knee. *Arthritis Rheumatol*. 2020;72(2):220–33.
31. MacKay C, Hawker GA, Jaglal SB. How do physical therapists approach management of people with early knee osteoarthritis? A qualitative study. *Phys Ther*. 2020;100(2):295-306.
32. Maly MR, Marriott KA, Chopp-Hurley JN. Osteoarthritis year in review 2019: Rehabilitation and outcomes. *Osteoarthritis Cartilage*. 2020;28(3):249-266.
33. Gaul C, Eschaliere A. Dose can help to achieve effective pain relief for acute mild to moderate pain with over-the-counter paracetamol. *The Open Pain Journal*. 2018;11:12-20.
34. Dhillon S. Tramadol/paracetamol fixed-dose combination: A review of its use in the management of moderate to severe pain. *Clin Drug Investig*. 2010;30(10):711–38.
35. Rawal N, Macquaire V, Catalá E, Berti M, Costa R, Wietlisbach M. Tramadol/paracetamol combination tablet for postoperative pain following ambulatory hand surgery: A double-blind, double-dummy, randomized, parallel-group trial. *J Pain Res*. 2011;4:103-10.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of the publisher and/or the editor(s). This publisher and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

© Copyright (2024): Author(s). The licensee is the journal publisher. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:

<https://www.sdiarticle5.com/review-history/125154>