International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 8, 20285
https://theaspd.com/index.php

Exploring Diabetes Mellitus Impact On Maxillary Or Mandibular Bone Density In Edentulous Patients: A Systematic Review

Nurul Auliya[1*], Eri Hendra Jubhari[2*], Muhammad Ikbal[2]
[1]Resident of Prosthodontic Department, Faculty of Dentistry, Hasanuddin University, Makassar, Indonesia
[2]Prosthodontic Department, Faculty of Dentistry, Hasanuddin University, Makassar, Indonesia

Abstract
Objective: *This systematic review assesses the impact of Diabetes Mellitus (DM) on maxillary and mandibular bone density in edentulous patients, focusing on the relationship between DM and bone mineral density (BMD) alterations and the implications for dental rehabilitation.*
Methods: *A systematic search was conducted in PubMed, ScienceDirect, and Wiley Online Library using keywords like "Diabetes Mellitus," "Bone Density" and "Maxillary and Mandibular" and "Edentulous." Studies published between 2014 and 2024 were reviewed according to PRISMA guidelines. The risk of bias was evaluated using the Joanna Briggs Institute (JBI) tools.*
Results: *The initial search identified 48 articles, 38 of which remained after duplicate removal. After screening titles and abstracts, 26 articles were selected for full-text review, resulting in 18 retrieved. Following inclusion criteria, 13 studies were excluded, leaving 5 for analysis. Three studies reported no significant differences in BMD between diabetic and non-diabetic groups, while two found significantly lower BMD in specific regions, such as the lingual cortical plate and trabecular regions, in diabetic patients.*
Discussion: *DM affects BMD with significant variability. Some studies found no significant differences, while others observed lower BMD in certain areas. This variability highlights the need for further research. Reduced BMD complicates denture placement and increases the risk of fractures and implant failure. Effective glycemic control is crucial for maintaining bone health and ensuring successful dental rehabilitation.*
Conclusion: *DM patients exhibit significant variability in BMD, underlining the need for tailored clinical approaches in dental rehabilitation.*
Keywords: *Bone Density, Diabetes Mellitus, Edentulous, Maxilla, Mandibula*

INTRODUCTION

Diabetes mellitus (DM) is a complex metabolic disorder characterized by chronic hyperglycemia due to impaired insulin production or function. It is a common health problem with significant health and economic impacts worldwide. Diabetes mellitus consists of several types with different pathophysiologies.[1,2] Type 1 diabetes mellitus (T1DM) is an autoimmune condition in which the immune system attacks pancreatic beta cells, resulting in insufficient insulin production. Type 1 diabetes mellitus is often diagnosed in childhood or adolescence and requires lifelong insulin therapy.[3-5] Meanwhile, type 2 diabetes mellitus (T2DM) is characterized by insulin resistance that eventually leads to insulin deficiency. Type 2 diabetes mellitus is often associated with obesity and lifestyle, is more common in adults but is increasingly found in younger populations due to rising obesity rates. Gestational diabetes mellitus (GDM), on the other hand, occurs during pregnancy and usually resolves after delivery, although this condition may increase the risk of developing T2DM later in life.[6-8]

One of the complications associated with DM is decreased bone density, which can affect the stability of the maxillary and mandibular bones. Decreased bone density in patients with DM can increase the risk of fractures and other complications, especially in the context of complete denture and implant use.[9-11] The use of dentures in patients with DM has become common practice to restore masticatory function and aesthetics. However, there is concern that the use of a denture may accelerate the process of bone resorption, especially in patients with poor glucose control.[11] This is due to the mechanical stress exerted by the dentures on the

bone surface, which may result in a further decrease in bone density, especially in patients with DM who already have bone-related metabolic disorders.[12-14]

Bone density in the maxilla and mandible of denture wearers is an important factor affecting the overall success of oral care. Bone density in these areas can vary significantly based on several factors, including age, gender, and edentulism. The mandible generally shows higher bone density compared to the maxilla. This is evident in cortical and cancellous bone measurements, with the mandible showing a progressive increase in density from anterior to posterior regions. [15-17] Cortical bone density in the mandible ranged from 800 to 1580 Hounsfield units (HU), while that in the maxilla ranged from 810 to 940 HU, except for the maxillary tuberosity which had a much lower density.[18] Research conducted by Stefano et al[19] states that bone density is generally higher in men than women, the difference is not always statistically significant.[19]

The relationship between bone density and diabetes mellitus, especially T2DM, is complex and diverse. Research conducted by Zhang et al[20] showed that T2DM can affect bone mineral density (BMD) through various mechanisms, leading to increased and decreased BMD in different contexts. This relationship is influenced by factors such as age, diabetes duration, insulin resistance, and oxidative stress.[21] Another study conducted by Luo et al[22] involving elderly men and post-menopausal women, found that BMD was higher in those with T2DM. However, this condition is accompanied by an increased risk of fractures over time, which is due to the prolonged duration of diabetes and insulin resistance.

Currently, research on mandibular bone density in patients with diabetes mellitus, especially in edentulous total patients, is very limited. Generally, existing studies only measure bone density at a single point in time, thus not providing a comprehensive picture of the gradual changes in bone density. This highlights the need for further research to explore how diabetes mellitus influences bone density changes over time in edentulous patients. Therefore, this systematic review was initiated with the aim of analyzing these changes in bone density more comprehensively in order to provide a deeper and more useful understanding in a medical and clinical context.

METHODS

This systematic review was conducted according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines for reporting studies evaluating healthcare interventions. Research question: Is there an effect of DM on bone density in patients with edentulism?

A focus question was designed following the PICO format as per the following patient/population, intervention, comparisons, and outcomes: (P) Edentulous patient with diabetes mellitus; (I) Diabetes mellitus; (C) Non-Diabetic Edentulous Patients; (O) Bone Density Changes in Maxillary or Mandibular Region (Houndsfield Unit dan QUS). The risk of bias was assessed using the Joanna Briggs Institute (JBI) tools checklist for analytical cross-sectional studies, evaluating sampling methods, data collection, and potential conflicts of interest.

The electronic search was performed by entering the combination of the following MeSH terms: “Bone Mineral Density” or “Bone Density” and “Diabetes mellitus” and “Maxillary and Mandibular” and “Edentulous patient”. The following electronic databases were screened for potential study articles: PubMed, Science Direct, and Google Scholar. The results were limited to studies written in English. The inclusion and exclusion criteria in this systematic review were the following:

Inclusion Criteria :

- Edentulous patients with diabetes mellitus.
- Randomized control trial
- Observational studies, such as cross-sectional, cohort, or case-control studies.
- Assessment of bone density in the maxillary and mandibular areas using CBCT and QUS
- Articles published in English
- Articles from 2014-2024

Exclusion Criteria

- Review studies (e.g., meta-analyses, previous systematic reviews, or review articles).

- Studies that did not report sufficient data on bone density in the maxilla and mandible.
- Studies published before 2014
- Unaccessible full text

The selection was performed independently by two independent (NA and EHJ) reviewers through titles and abstracts of all identified studies through an electronic search read individually by the authors. For the studies that appeared to fulfill the inclusion criteria or those studies that had limited data in the title and abstract to reach the final decision, the full record was gathered. Disagreements among authors were resolved after discuss

RESULT

The literature search was conducted using the specified terms across the mentioned electronic databases. The flowchart detailing the literature search and selection process is shown in Figure 1. The initial search identified 48 articles, 38 of which remained after duplicate removal. After screening titles and abstracts, 26 articles were selected for full-text review, resulting in 18 retrieved. Following the inclusion criteria, 13 studies were excluded, leaving 5 for analysis, as summarized in Table 1.

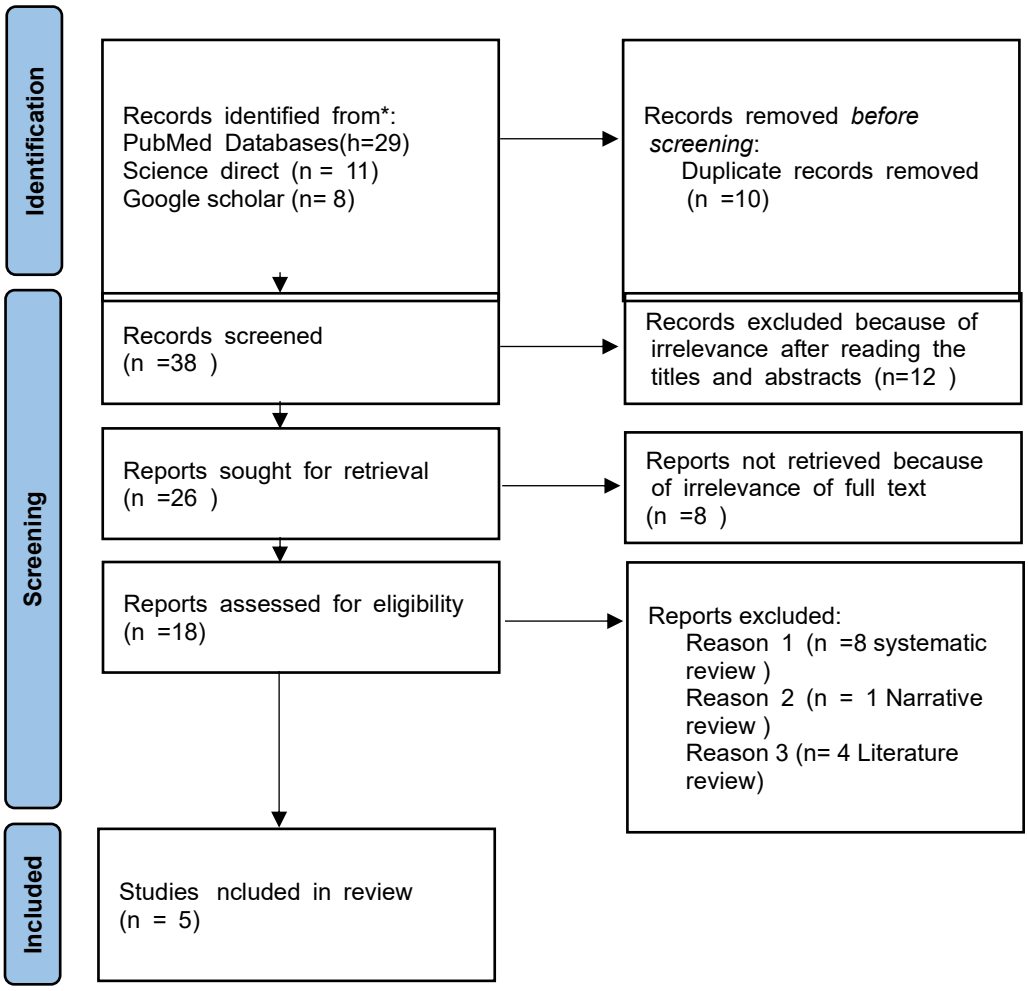

Figure 1. PRISMA Flow Chart

Table 1. Summary of the studies

Author	Country	Study design	Population	Diabetic Group Definition	Bone density assessment	Bone Region	Diabetic Group BMD (Mean ± SD in Hounsfield Units)	Non-Diabetic Group BMD (Mean ± SD in Hounsfield Units)	Main Finding
Jolly SJ, et al (2015)[23]	India	Cross-sectional	40 (20 T2DM, 20 control)	HbA1c 6.1%-8% (controlled T2DM)	Spiral CT	Trabecular (Mandibular)	498.12 ± 32.59	514.31 ± 20.03	No significant differences in BMD between controlled T2DM and non-diabetic men.
Patil SM, et al (2021)[24]	India	Cross-sectional	60 (30 T2DM, 30 control)	HbA1c 6.1%-8% (controlled T2DM)	CBCT	Trabecular (Maxillary)	445.06 ± 20.64	464.04 ± 40.05	No significant difference in BMD between groups.
Dahihandekar C, et al (2022)[25]	India	Cross-sectional	40 (20 T2DM, 20 control)	HbA1c 6.1%-8% (T2DM), 50-65 years	CBCT	Trabecular (Maxillary)	590.75 ± N/A	636.58 ± N/A	T2DM group had significantly lower BMD at lingual and trabecular sites, but no difference at buccal cortical plates.
Khandelwal N, et al (2023)[26]	India	Cross-sectional	850 (425 T2DM, 425 control)	T2DM >5 years, HbA1c 8.0 ± 1.14%	Quantitative Ultrasound (QUS)	Calcaneus (Overall)	-4.3 ± 1.23	-2.6 ± 0.34	Diabetics had significantly lower BMD than controls; recommends osteoporosis screening for T2DM.

Number	Author and Year of Article	Criteria Based on Questions in Checklist Form								Score (%) Category of bias
		Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	
1	Jolly SJ, et al (2015)[23]	√	√	√	√	√	√	√	X	87.5% (Low risk)
2	Patil SM, et al (2021)[24]	√	√	√	√	√	√	√	X	87.5% (Low risk)
3	Dahihandekar C, et al (2022)[25]	√	√	√	√	√	√	√	X	87.5% (Low risk)
4	Khandelwal N, et al (2023)[26]	√	√	√	√	√	√	√	X	87.5% (Low risk)
5	Patil SM, et al (2024)[27]	√	√	√	√	√	√	√	X	87.5% (Low risk)

Patil SM, et al (2024)[27]	India	Cross-sectional	60 (30 T2DM, 30 control)	HbA1c 6.1%-8% (controlled T2DM)	CBCT	Trabecular (Maxillary)	590.75 ± N/A	636.58 ± N/A	No significant difference in BMD between controlled T2DM and non-diabetic groups.

Table 1 presents a summary of the five studies included in this systematic review. The results of these studies revealed varying findings regarding bone mineral density in controlled type 2 diabetic patients compared to non-diabetic controls. Jolly SJ et al. (2015) and Patil SM et al. (2021) found no significant changes in bone mineral density between controlled diabetic and non-diabetic subjects. Similarly, Patil SM et al. (2024) also reported no significant differences in bone mineral density between non-diabetic and controlled diabetic subjects. In contrast, Dahihandekar C et al. (2022) observed that individuals with type 2 diabetes mellitus exhibited significantly lower bone mineral density in the lingual cortical plate and trabecular region, while the buccal cortical region showed no changes. Khandelwal N et al. (2023) also found that type 2 diabetes mellitus was associated with significantly lower bone mineral density (BMD) compared to non-diabetic individuals. These findings suggest that while some studies found no difference, others highlighted a notable reduction in bone mineral density in specific regions of the bone in diabetic patients.

DISCUSSION

Diabetes mellitus (DM) has a significant impact on the density and quality of both maxillary and mandibular bones, primarily through mechanisms that alter bone metabolism and microarchitecture.[28,29] Both type 1 (T1DM) and type 2 diabetes mellitus (T2DM) are linked to increased bone fragility, though the specific effects on bone density may differ between the two types.[30-32] The influence of DM on bone density is complex, involving changes in bone mineral density (BMD), alterations in bone turnover, and the accumulation of advanced glycation end-products (AGEs), all of which contribute to weakened bone strength and an elevated risk of fractures.[33,34]

In this study, two studies found that type 2 diabetes mellitus (T2DM) was associated with significantly lower bone mineral density (BMD) compared to non-diabetic individuals.[25,26] This finding aligns with research by Nugroho et al.[35], which reported a decrease in BMD among T2DM patients, particularly in older adults. This study found that 61% of T2DM patients had decreased BMD, with a higher prevalence in those over 60 years old.[35] Additionally, research conducted at Zagazig University Hospitals found that BMD was significantly decreased among diabetic patients compared to non-diabetics, with a higher incidence of osteopenia and osteoporosis among diabetics.[36] In contrast, some research indicates that T2DM patients may have higher BMD. A study by Alshomar et al.[37] found higher bone mineral density (BMD) in the lumbar spine among diabetic patients compared to non-diabetic individuals.[37] Similarly, a Mendelian randomization study by Qu et al.[38] suggested that type 2 diabetes mellitus (T2DM) is positively associated with BMD at specific sites, such as the femoral neck and heel.[38] Furthermore, studies by Guan et al.[9] also identified a positive association between T2DM and increased BMD, particularly in the elderly population.[9]

However, this study also found no significant difference in bone mineral density (BMD) between nondiabetic and controlled diabetic subjects. [23, 24, 27] This finding is consistent with several studies that have reported no significant difference in BMD between diabetic and non-diabetic groups. For example, a study by Daud et al.[39] using quantitative computed tomography (QCT) found no significant difference in BMD scores between the two groups, although it did note a higher incidence of osteoporosis among diabetics.[39] Similarly, research conducted in South Karnataka and Western Odisha using qualitative ultrasound found no significant difference in BMD between diabetics and non-diabetics. However, a higher incidence of osteoporosis was observed in diabetic subjects, suggesting that while BMD may not differ significantly, the risk of osteoporosis could be higher in diabetics.[40,41]

Several factors influence bone mineral density (BMD) in diabetic patients, with age and duration of diabetes being particularly significant. Older age and longer duration of diabetes are associated with decreased BMD and an increased risk of fractures. Poor glycemic control and insulin resistance further contribute to lower BMD and a higher fracture risk in type 2 diabetes mellitus (T2DM) patients.[42] The effects of anti-diabetic medications on BMD vary, with some medications potentially increasing BMD, while others have no significant impact.[43,44] The prevalence of osteoporosis in T2DM patients also shows inconsistencies, with some studies indicating a lower risk compared to non-diabetics, while others suggest a higher risk, particularly with prolonged diabetes duration.[37,45] Diabetes mellitus leads to an imbalance in bone remodeling, characterized by reduced bone formation and increased resorption. This is partially due to the formation of

advanced glycation end-products (AGEs) that impair bone collagen properties. Furthermore, insulin deficiency and altered hormone levels contribute to these changes, affecting overall bone density and quality.[46-48]

Histological studies in T2DM patients reveal increased activity of osteoblastic cells and the presence of weakly mineralized osteoid, indicating heightened bone metabolic processes. While there may be attempts at bone formation, the quality of newly formed bone appears compromised.[49] Despite potentially higher BMD in some T2DM patients, the risk of fractures remains elevated due to poor bone quality and increased fall risk. To address these challenges, regular osteoporosis screening is recommended for T2DM patients to detect early bone loss, with the trabecular bone score (TBS) being suggested as a more reliable diagnostic tool than BMD alone for assessing bone quality.[26,50] Preventive strategies, including early intervention, lifestyle modifications, and appropriate medication use, are crucial to preventing osteoporosis and fractures in T2DM patients.[51] Bone mineral density assessments using cone-beam computed tomography (CBCT) and dual-energy X-ray absorptiometry (DEXA) reveal a strong correlation between glycemic control (measured by HbA1c levels) and mandibular BMD. Poorly controlled diabetes is associated with lower BMD, emphasizing the importance of glycemic management in maintaining bone health.[52,53]

Despite the challenges identified, effective management strategies, such as optimal glycemic control and thorough pre-operative assessments, can help mitigate some of the adverse effects of diabetes on bone density, ultimately improving outcomes for dental treatments. Advanced imaging techniques, such as cone-beam computed tomography (CBCT), play a pivotal role in accurately assessing bone quality, thereby aiding in better treatment planning and management for diabetic patients. However, the limitations of this systematic review include the heterogeneity of the included studies, which varied in methodology and diagnostic tools used to assess bone mineral density (BMD). Variations in imaging methods, such as CBCT, dual-energy X-ray absorptiometry (DEXA), and quantitative computed tomography (QCT), may have contributed to inconsistencies in the results. Moreover, discrepancies in the definition and diagnosis of osteoporosis, as well as the lack of uniformity in classifying diabetes severity, further complicate the interpretation of the findings. Another limitation is the potential for publication bias, where studies with significant findings are more likely to be published, leading to an overrepresentation of positive results. Additionally, the long-term impact of diabetes management strategies, including glycemic control and medication use, on bone density remains underexplored, highlighting the need for further prospective and large-scale studies. Lastly, this review primarily focuses on observational studies, limiting the ability to establish causality between diabetes and bone mineral density. Therefore, more randomized controlled trials and longitudinal studies are needed to provide stronger evidence regarding the relationship between diabetes mellitus and bone health, particularly in edentulous patients.

CONCLUSION

The results of this systematic review indicate that patients with diabetes mellitus (DM) exhibit significant variability in bone mineral density (BMD). While some studies report reduced BMD, particularly in the mandibular region, others show higher or stable BMD compared to non-diabetic individuals. These discrepancies highlight the need for standardized methodologies and larger, more controlled studies to comprehensively understand the impact of diabetes on bone health. Given the complications associated with lower BMD, such as an increased risk of fractures and implant failures, the findings stress the importance of utilizing both Dual-Energy X-ray Absorptiometry (DEXA) and Cone Beam Computed Tomography (CBCT) for a thorough evaluation and management of bone health in diabetic patients.

Future research should investigate the long-term effects of glycemic control and diabetes management on BMD, explore the role of CBCT in assessing bone quality, and establish unified protocols for BMD assessment in clinical practice. A deeper understanding of bone density dynamics in DM patients will enable the development of better preventive and therapeutic strategies, ultimately improving clinical outcomes and the quality of life for these patients.

Acknowledgment
I am deeply grateful to my supervisor, Eri Hendra Jubhari, drg., M.Kes., Sp. Pros (K), for his guidance and for sharing his valuable experiences in writing this paper. We confirm that the manuscript has been read and approved by all named authors.
Conflict of Interest: No conflict of interest was declared by the author.

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