

RESEARCH ARTICLE

## Differences in bone quality and condylar head shape between patients with type 2 diabetes mellitus and non-diabetic patients

Rahmi Amalia\*✉, Teuku Harqad\*, Lusi Epsilawati\*\*, Merry Damayanti\*\*, Rohmat Nursin\*\*\*

\*Dentomaxillofacial Radiology Specialty Program, Faculty of Dentistry, Universitas Padjadjaran, Bandung, West Java, Indonesia

\*\*Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Universitas Padjadjaran, Bandung, West Java, Indonesia

\*\*\*Primary Care Department, Faculty of Dentistry, SEGi University, Petaling Jaya, Malaysia

\*JI Sekeloa Selatan I, Bandung, West Java, Indonesia; ✉ correspondence: [drg.rahmiamaliaa@gmail.com](mailto:drg.rahmiamaliaa@gmail.com)

Submitted: 7<sup>th</sup> January 2025; Revised: 9<sup>th</sup> July 2025; Accepted: 6<sup>th</sup> August 2025

### ABSTRACT

This study aimed to compare bone quality—assessed through mandibular bone density—and condylar head shape between patients with type 2 diabetes mellitus (DM) and non-diabetic (non-DM) individuals, using bone histogram values derived from panoramic radiographs. An observational descriptive design with a cross-sectional approach was employed. The study population comprised all panoramic radiographic records collected during the study period. The sample consisted of 25 radiographs: 11 from male patients (DM and non-DM) and 14 from female patients (DM and non-DM), aged 40–60 years. Bone density was measured using a histogram analysis within a 4 × 4 mm region of interest (ROI) in the condylar head area, and the condylar head shape was also evaluated. Statistical analysis was subsequently performed. The findings revealed no statistically significant difference in mandibular bone density in the condylar area between DM and non-DM patients ( $p > 0.005$ ). Similarly, the condylar head shape was predominantly oval in both groups. While individuals with type 2 DM tended to exhibit lower bone density values than non-DM individuals, the difference was not statistically significant. No significant differences in bone density were observed between the left and right condylar heads. However, variations in condylar head morphology were noted.

**Keywords:** bone density; condylar head shape; mandible; panoramic radiographs; type 2 diabetes mellitus

Copyright: © 2025, Majalah Kedokteran Gigi Indonesia (CC BY-NC-SA 4.0)

### INTRODUCTION

The World Health Organization (WHO) defines diabetes mellitus (DM) as a chronic metabolic disease characterized by elevated blood glucose levels, with more than 90% of cases classified as type 2 DM.<sup>1,2,3,4</sup> Type 2 DM is marked by reduced insulin secretion due to pancreatic  $\beta$ -cell dysfunction, leading to tissue insulin resistance (IR) and an inadequate insulin secretory response.<sup>5,6,7</sup> As the disease progresses, declining insulin levels disrupt glucose homeostasis, resulting in hyperglycemia. Most individuals with type 2 DM present with obesity or an increased percentage of body fat, particularly in the abdominal region.<sup>5,8,9</sup>

According to the International Diabetes Federation (IDF), DM was the cause of approximately 4.2 million deaths worldwide in 2019. That year, an estimated 463 million adults

(aged 20–79 years) were living with DM, a figure projected to rise to 700 million by 2045. The highest prevalence occurs among individuals aged 40–59 years. More than 80% of type 2 DM cases are found in low- to middle-income countries, including Indonesia.<sup>5,10</sup>

The relationship between DM and bone density is complex and varies by DM type. Type 1 DM is generally associated with reduced bone mineral density (BMD) and an increased fracture risk.<sup>5,6</sup> In contrast, type 2 DM often presents with higher BMD—particularly in the femoral neck, hip, and spine—yet paradoxically carries an elevated fracture risk, likely due to an increased incidence of falls.<sup>7,8</sup> Factors influencing BMD in type 2 DM include age, sex, body mass index (BMI), and glycemic control.<sup>9</sup> Pathophysiological mechanisms may involve advanced glycation

end products, microarchitectural alterations, and changes in bone turnover. Antidiabetic medications can also affect bone health: thiazolidinediones have been linked to increased fracture risk, whereas metformin and sulfonylureas appear to have minimal impact on bone quality in some studies.<sup>6,7</sup> Consequently, early screening for fracture risk is recommended for patients with systemic conditions such as type 2 DM.<sup>8,9,10</sup>

The temporomandibular joint (TMJ) is a component of the mandibular bone and the only joint in the craniofacial region.<sup>11</sup> Reduced bone quality can affect both the morphology and density of this structure, as well as the mandible in general.<sup>11,12,13</sup> Bone density can be evaluated through histogram analysis of radiographs, which quantifies grayscale intensity as a proxy for mineral density.<sup>11,14</sup> Panoramic radiographs are frequently used for jawbone assessment, as many healthcare facilities employ them as a standard diagnostic tool prior to treatment.<sup>15,16</sup> These radiographs offer a wide field of view with minimal radiation exposure. Bone morphology analysis, including the assessment of mandibular cortical index (MCI) for conditions such as osteoporosis, is often conducted using panoramic images.<sup>16,17,18</sup>

The present study aimed to evaluate mandibular bone density in the TMJ region by measuring bone density in the condylar head and assessing condylar head morphology in patients with type 2 DM and non-DM individuals, using panoramic radiographs analyzed with ImageJ software.

## MATERIALS AND METHODS

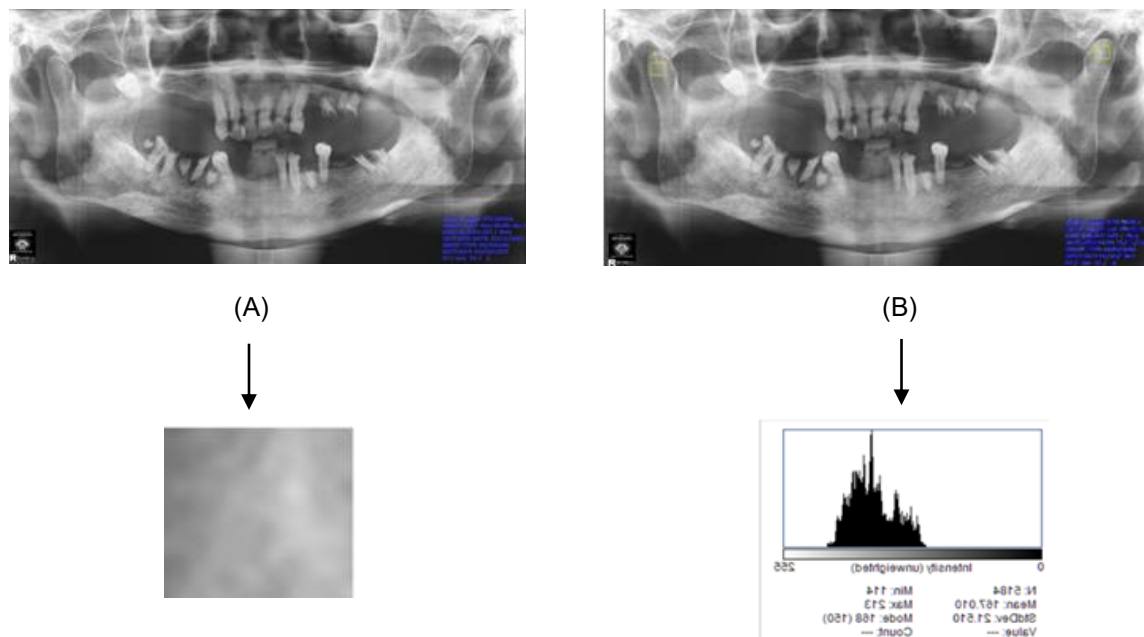
This study utilized an observational descriptive design with a cross-sectional approach. The study population comprised panoramic radiographic records from patients who visited diabetes specialty clinics in Cimahi and Padalarang, Bandung, West Java, during the research period. Type 2 diabetes mellitus (DM) was confirmed through medical records, and all participants provided informed consent. Radiographs were obtained at RSGM Unjani Cimahi.

Secondary data from 50 panoramic radiographs were analyzed, consisting of 25 type 2 DM patients and 25 non-DM patients. Each group included 11 males and 14 females, aged 40–60 years. Exclusion criteria included: (1) panoramic radiographs that could not be interpreted, (2) radiographs showing mandibular diseases or fractures, and (3) distorted images in which the size or shape of the structures differed from the original anatomy. Non-DM radiographs were selected from the researchers' archives, matched in number and demographic characteristics to the DM group.





The bone density of the condylar head region was analyzed bilaterally (left and right). Measurements were performed using ImageJ software, applying histogram analysis to a 4 × 4 mm region of interest (ROI) in the condylar head area (Figures 1 and 2). The mean (± SD) grayscale values were recorded for the right and left condyles in both DM and non-DM groups, stratified by sex.



**Figure 1.** Analysis area in the condylar region using a 4 × 4 mm ROI.



**Figure 2.** Bone density analysis with ImageJ on panoramic radiography: (A) cropped area with a 4 × 4 mm ROI; (B) histogram of density values within the ROI in the condylar region.

Radiograph	Description
	Ovoid Shape (Shape 1): Narrower neck with an expanded superior surface.
	Pointed Shape (Shape 2): Superior surface forms a diamond-like angle.
	Angled Shape (Shape 3): The junction between the neck and condylar head forms an angle resembling a bird's beak.
	Flat Shape (Shape 5): Superior surface is flat.

**Figure 3.** Condylar head shapes analyzed in this study.

Condylar head morphology was assessed visually. One researcher served as the intra-observer, and two radiology-specialist dentists acted as extra-observers. Disagreements were resolved by consensus. Morphological categories

included ovoid, pointed, angled, and flat shapes (Figure 3).<sup>19</sup>

All data were analyzed using IBM SPSS Statistics (version XX; IBM Corp., Armonk, NY, USA). The normality of bone density values was

assessed using the Shapiro–Wilk test. For normally distributed data, an independent sample t-test was performed to compare mean bone density values between the type 2 diabetes mellitus (DM) group and the non-DM group.

The primary quantitative variable was the mean grayscale value (bone density) in the condylar head region, measured independently for the right and left condyles. Each side was analyzed separately to assess potential side-specific differences, and an overall mean was subsequently calculated from both sides. A p-value of  $< 0.005$  was considered statistically significant. In addition to quantitative analysis, condylar head morphology was evaluated descriptively. The frequency and percentage of each morphological

type were tabulated for both DM and non-DM groups. No inferential statistics were applied for morphology, as the objective was to provide a qualitative overview of shape variations.

## RESULTS

This study examined differences in condylar bone density and morphology between patients with type 2 DM and non-DM individuals:

**Table 1.** Sample characteristics

	Type-2 DM patients	Non-DM patients
Male	11	11
Female	14	14

**Table 2.** Descriptive analysis of bone density in type 2 DM and non-DM groups

ROI area	Right condyle		Left condyle	
	DM	Non-DM	DM	Non-DM
Min	87	67	80	76
Max	187	184	183	185
Mean	129.2 $\pm$ 21.0	134.52 $\pm$ 21.53	129.96 $\pm$ 21.48	133.36 $\pm$ 22.34
Std. deviation	21.00595	21.53509	21.48154	22.34554

**Table 3.** Normality test results for type 2 DM and Non-DM groups

ROI area		Right condyle		Left condyle	
		Type-2 DM patients	Non-DM patients	Type-2 DM patients	Non-DM
Shapiro-Wilk	Statistic	0.960	0.920	0.983	0.974
	df	25	25	25	25
	Sig.	0.416	0.51	0.934	0.756

**Table 4.** Homogeneity test of type 2 DM and Non-DM patients

Independent samples test		
		Sig.
Right condyle	Equal variances assumed	0.867
Left condyle	Equal variances assumed	0.856

The sample comprised 50 panoramic radiographs: 25 from type 2 DM patients and 25 from non-DM patients. Each group consisted of 11

males and 14 females. Most participants ( $n = 10$ ) were aged 45–56 years, while the remainder were between 40–44 and 57–60 years old. Age and sex

**Table 5.** Independent samples t-test results for all groups

Independent samples test		t-test for equality of means		
		t	p value (2-tailed)	Std. error difference
Right condyle	Equal variances assumed	- 0.884	0.381	± 6.01668
	Equal variances not assumed	- 0.884	0.381	± 6.01668
Left condyle	Equal variances assumed	- 0.548	0.586	± 6.19929
	Equal variances not assumed	- 0.548	0.586	± 6.19929

**Table 6.** Observation results for condylar head shape

	DM		Normal	
	Left	Right	Left	Right
Flattened	5	2	0	0
Angled	5	8	5	6
Ovoid	15	15	20	19
Bird beak	0	0	0	0

characteristics were not included as covariates in further analyses.

The mean right condyle density in DM patients was 129.20 (SD = 21.00), with values ranging from 87 to 187. There was no statistically significant difference in bone density between DM and non-DM patients.

Normality testing using the Kolmogorov–Smirnov (K–S) test was performed. The decision criteria were as follows: (1) If the asymp. sig. (2-tailed) value is greater than 0.05, the data are considered normally distributed. (2) If the asymp. sig. (2-tailed) value is less than 0.05, the data are considered not normally distributed.

In Table 3, the normality test results show that the right and left condyle data in both type 2 DM and non-DM patients have significance values greater than 0.05, indicating that the bone density data for both sides are normally distributed.

Following the normality test, a homogeneity test was performed to determine whether the variances between groups were equal. This test was conducted using Levene's test in the SPSS Statistics software (version 27; IBM Corp., Armonk, NY, USA).

Table 4 shows that, in all data groups, both right and left condyles have p-values greater than 0.05. This indicates that the data are homogeneous, meeting the assumption required for subsequent comparative testing. The difference test was conducted using the independent samples t-test. A statistically significant difference was defined as a p-value (2-tailed) < 0.05.

The t-test results in Table 5 show no statistically significant differences in bone density between the groups. The small numerical differences observed may reflect minimal true differences that were insufficient to reach statistical significance.

Based on morphological observations, both the type 2 DM and non-DM groups were predominantly characterized by ovoid and angled condylar head shapes. The flat condylar head shape appeared only in the type 2 DM group, while neither group exhibited the bird-beak (pointed) condylar head shape.

## DISCUSSION

Type 2 diabetes mellitus (DM) and osteoporosis are among the most common systemic metabolic disorders worldwide. Type 2 DM results from a

combination of two primary factors: insufficient insulin secretion by pancreatic  $\beta$ -cells and the inability of body tissues to respond adequately to insulin.<sup>20,21,22</sup> Insulin release and activity must precisely match the body's metabolic demands; when this process fails, multiple metabolic pathways—including bone remodeling—are disrupted. Osteoporosis is a systemic metabolic bone disease characterized by reduced bone mass and microstructural deterioration, leading to increased fracture risk.<sup>23,24,25,26</sup> Metabolic disturbances are a hallmark of type 2 DM and may manifest as decreased bone density. Although type 2 DM is associated with impaired bone homeostasis, several studies from Korea have reported no significant difference in spinal or lumbar bone density between type 2 DM and non-DM groups.<sup>22,23,24,26</sup>

Diabetes is strongly associated with changes in bone metabolism, adversely affecting bone and calcium regulation, which in turn influence carbohydrate, protein, and lipid metabolism. While bone metabolism is altered in type 2 DM, bone mineral density (BMD) often remains stable. This is consistent with the present findings, in which no significant difference was observed in condylar bone density between type 2 DM and non-DM patients ( $p > 0.005$  for all comparisons). Minor numerical differences in bone density may reflect the small sample size or a true absence of difference.

These results align with the findings of Liu et al, who reported no decrease in BMD in type 2 DM patients,<sup>27</sup> and contrast with Jang et al, who found reduced BMD in this population. Sosa et al similarly reported no significant change in BMD in patients with type 2 DM.<sup>28</sup> Although low BMD is a recognized contributor to adverse health outcomes, early detection of bone loss in type 2 DM patients is critical for preventing fractures.<sup>20</sup>

Several studies have also demonstrated a significant association between type 2 DM and temporomandibular joint (TMJ) disorders. Patients with type 2 DM exhibit more severe TMJ dysfunction compared to non-diabetic individuals, with peripheral diabetic neuropathy identified as an independent risk factor.<sup>29</sup> Diabetes may alter condylar adaptation during mandibular

development, reduce bone density, and influence the expression of matrix metalloproteinases and their tissue inhibitors.<sup>30</sup> Cone-beam computed tomography has revealed reduced jawbone tissue density in diabetic patients, particularly in the condylar region, suggesting compromised bone quality.<sup>31</sup> Furthermore, condylar morphology is strongly associated with TMJ status in adult women, as assessed via panoramic radiography. These findings highlight the complex interplay between diabetes and TMJ health, emphasizing the importance of considering diabetes status in TMJ evaluation and management.<sup>32</sup>

The temporomandibular joint (TMJ), as the only synovial joint in the craniofacial region, possesses considerable mobility and may be affected by the systemic progression of type 2 diabetes mellitus (DM). The pathophysiology of DM is closely linked to insulin production by pancreatic  $\beta$ -cells. Before insulin is produced, it is first synthesized as pre-proinsulin, which is subsequently modified to form proinsulin.<sup>33,34</sup> Proinsulin is then translocated from the endoplasmic reticulum (ER) to the Golgi apparatus (GA), where it enters immature secretory vesicles and is cleaved into C-peptide and insulin.<sup>33,35,36</sup> Mature insulin is stored in granules until it is released in response to stimuli—most notably, elevated blood glucose concentrations.

When glucose levels rise,  $\beta$ -cells take up glucose primarily via glucose transporter 2. Once internalized, glucose undergoes catabolism, increasing the intracellular ATP/ADP ratio. This rise in ATP leads to the closure of ATP-sensitive potassium channels in the plasma membrane, causing depolarization and the opening of voltage-dependent calcium channels. The influx of calcium increases intracellular calcium concentration, which triggers the fusion of insulin-containing granules with the plasma membrane, resulting in insulin exocytosis.<sup>37,38,39</sup> Calcium plays a critical role in stimulating insulin secretion, and impaired calcium signaling can disrupt this process. When calcium receptor activity increases abnormally, intracellular calcium reserves may become depleted, potentially contributing to reduced bone density.<sup>40</sup>



In the present study, no notable changes were observed in the overall shape of the condylar head between type 2 DM and non-DM groups. In both groups, the condylar head was predominantly ovoid—approximately 15–20 condyles—followed by the angled form—approximately 8–5 condyles. Only the DM group exhibited flat condylar shapes. These findings suggest that reduced bone density in the condylar head region does not necessarily correspond to alterations in condylar morphology. This aligns with previous studies by Sonal V (2016) and Suhartini (2011), which reported that condylar head shape is influenced by multiple factors, including TMJ physiology and temporomandibular disorders, rather than bone density alone.<sup>41,42</sup>

## CONCLUSION

This study found no statistically significant difference in mandibular condylar bone density between patients with type 2 DM and non-DM individuals, with both groups demonstrating comparable mean grayscale values in the condylar region. However, morphological assessment revealed a greater tendency toward flattened condylar shapes in the type 2 DM group compared to the non-DM group. This variation may indicate early degenerative or remodeling changes in the TMJ associated with systemic metabolic alterations in diabetic patients. Further studies with larger sample sizes and advanced morphometric analysis are warranted to validate these findings.

## ACKNOWLEDGMENTS

This research was self-funded and received no financial support from external sources.

## CONFLICTS OF INTEREST

The author declares no conflicts of interest related to this study.

## REFERENCES

1. Singh N, Kesharwani R, Tiwari AK, Patel DK. A review on diabetes mellitus. *The Pharma Innovation Journal*. 2016; 5(7): 36-40.
2. Shotliff K. *Diabetes mellitus*. Oxford Medicine Online; 2018.
3. Goldenberg RM, Punthakee Z. Definition, classification and diagnosis of diabetes, prediabetes and metabolic syndrome. *Can J Diabetes*. 2018; 42 (Suppl 1): S10-15. doi: 10.1016/j.jcjd.2017.10.003
4. Petersmann A, Müller-Wieland D, Müller UA, Landgraf R, Nauck M, Freckmann G, Heinemann L, Schleicher E. Definition, classification and diagnosis of diabetes mellitus. *Exp Clin Endocrinol Diabetes*. 2019; 127(S01): S1-S7. doi: 10.1055/a-1018-9078
5. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C. Pathophysiology of type 2 diabetes mellitus. *Int J Mol Sci*. 2020; 21(17): 6275. doi: 10.3390/ijms21176275
6. Stumvoll M, Goldstein BJ, van Haefen TW. Type 2 diabetes: principles of pathogenesis and therapy. *Lancet*. 2005; 365(9467): 1333-1346. doi: 10.1016/S0140-6736(05)61032-X
7. Weyer C, Bogardus C, Mott DM, Pratley RE. The natural history of insulin secretory dysfunction and insulin resistance in the pathogenesis of type 2 diabetes mellitus. *J Clin Invest*. 1999; 104(6): 787-794. doi: 10.1172/JCI7231
8. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. *Lancet*. 2017; 389(10085): 2239-2251. doi: 10.1016/S0140-6736(17)30058-2
9. NCD Risk Factor Collaboration. Worldwide trends in diabetes since 1980: A pooled analysis of 751 population-based studies with 4.4 million participants. *Lancet*. 2016; 387(10027): 1513-1530. doi: 10.1016/S0140-6736(16)00618-8
10. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med*. 2003; 348(5): 383-393. doi: 10.1056/NEJMoa021778
11. Rachmawati N, Firman RN, Epsilawati L, Damayanti MA. Analysis of the panoramic radiographic density of the mandibular

- bone in the elderly due to increased cortisol levels. *Jurnal Radiologi Dentomaksilofasial Indonesia (JRDI)*. 2022; 6(2): 55-58.  
doi: 10.32793/jrdi.v6i2.885
12. Cahyaningsih MN, Saraswati LD, Yuliawati S, Wuryanto MA. Gambaran Densitas Mineral Tulang (DMT) pada Kelompok Dewasa Awal (19-25 Tahun) (Studi di Fakultas Kesehatan Masyarakat Universitas Diponegoro). *Jurnal Kesehatan Masyarakat*. 2017; 5(4): 424-430.  
doi: 10.14710/jkm.v5i4.18525
  13. Licata A. Bone density vs bone quality: what's a clinician to do?. *Cleve Clin J Med*. 2009; 76(6): 331-336. doi: 10.3949/ccjm.76a.08041
  14. Barlian B, Azhari, Pramanik F. Correlation between mandibular trabeculae bone density on panoramic radiograph and body mass index of men aged 5-35 years old. *Journal of Dentomaxillofacial Science*. 2018; 3(3): 166-168.
  15. Camargo AJ, Côrtes ARG, Aoki EM, Baladi MG, Arita ES, Watanabe PCA. Analysis of bone quality on panoramic radiograph in osteoporosis research by fractal dimension. *Applied Mathematics*. 2016; 7(4): 375-386.  
doi: 10.4236/am.2016.74035
  16. White SC. Oral radiographic predictors of osteoporosis. *Dentomaxillofac Radiol*. 2002; 31(2): 84-92. doi: 10.1038/sj.dmfr.4600674
  17. Horner K, Devlin H, Harvey L. Detecting patients with low skeletal bone mass. *J Dent*. 2002; 30(4): 171-175.  
doi: 10.1016/s0300-5712(02)00010-6
  18. Klemetti E, Kolmakov S, Kroger H. Pantomography in assessment of the osteoporosis risk group. *Scand J Dent Res*. 1994; 102(1): 68-72.  
doi: 10.1111/j.1600-0722.1994.tb01156.x
  19. Anjani KG, Nurrachman AS, Rahman FUA, Firman RN. Bentuk dan posisi kondilus sebagai marker pada Temporomandibular Disorder (TMD) melalui radiografi panoramik. 2020; 4(3): 91-100. doi: 10.32793/jrdi.v4i3.609
  20. Khandelwal N, Rajauria S, Kanjalkar S, et al. Bone mineral density evaluation among type 2 diabetic patients in rural haryana, india: an analytical cross-sectional study. *Cureus*. 2023; 15(9): e45908.  
doi: 10.7759/cureus.45908
  21. WHO: Diabetes fact sheet. 2023. Accessed: October 15, 2024: <https://www.who.int/news-room/factsheets/detail/diabetes>.
  22. Qiu J, Li C, Dong Z, Wang J. Is diabetes mellitus a risk factor for low bone density: a systematic review and meta-analysis. *BMC Endocr Disord*. 2021; 21(1): 65.  
doi: 10.1186/s12902-021-00728-3
  23. Paschou SA, Dede AD, Anagnostis PG, Vryonidou A, Morganstein D, Goulis DG. Type 2 diabetes and osteoporosis: a guide to optimal management. *J Clin Endocrinol Metab*. 2017; 102(10): 3621-3634.  
doi: 10.1210/jc.2017-00042
  24. Ali D, Tencerova M, Figeac F, Kassem M, Jafari A. The pathophysiology of osteoporosis in obesity and type 2 diabetes in aging women and men: The mechanisms and roles of increased bone marrow adiposity. *Front. Endocrinol*. 2022; 13: 981487.  
doi: 10.3389/fendo.2022.981487
  25. Kumari C, Yagoub GY, Ashfaque M, Jawed S, Hamid P. Consequences of diabetes mellitus in bone health: traditional review. *Cureus*. 2021; 13(3): e13820.  
doi: 10.7759/cureus.13820
  26. Ma L, Oei L, Jiang L, Estrada K, Chen H, Wang Z, Yu Q, Zillikens MC, Gao X, Rivadeneira F. Association between bone mineral density and type 2 diabetes mellitus: a meta-analysis of observational studies. *Eur J Epidemiol*. 2021; 27(5): 319 - 332.  
doi: 10.1007/s10654-012-9674-x
  27. Liu B, Liu J, Pan J, Zhao C, Wang Z, Zhang Q. The association of diabetes status and bone mineral density among US adults: evidence from NHANES 2005-2018. *BMC Endocr Disord*. 2023; 23(1): 27.  
doi: 10.1186/s12902-023-01266-w
  28. Sosa M, Dominguez M, Navarro MC, Segarra MC, Hernández D, de Pablos P, Betancor P: Bone mineral metabolism is normal in non-insulin-dependent diabetes mellitus. *J*



- Diabetes Complications. 1996; 10(4): 201-205. doi: 10.1016/1056-8727(95)00062-3
29. Alsaad LN, Abdulameer JA, Akolaa EA, Muttappallymyalil J, Sreedharan J. Bone mineral density and its determinants: a systematic review of risk factors and prevention strategies. *Biomed Pharmacol J*. 2023; 16(3): 1791-1796. doi: 10.13005/bpj/2758
  30. Lapina NV, Skorikova LA, Shabalina IM, Gerbova TV, Kochurova EV. Evaluation of pathological changes of the temporomandibular joint in patients with type 2 diabetes. *Russian Journal of Dentistry*. 2020; 24(3): 189-192. doi: 10.17816/1728-2802-2020-24-3-189-192
  31. Zhong X, Wang H, Jian X. Expression of matrix metalloproteinases-8 and -9 and their tissue inhibitors in the condyles of diabetic rats with mandibular advancement. *Exp Ther Med*. 2014; 8(5): 1357 - 1364. doi: 10.3892/etm.2014.1984
  32. Prozorova NV, Fadeyev R, Veber VR, Chibisova M, Prozorova IV, Sokolova SM, Tarasenko AS, Golubjatnikov MV. Computed tomography attenuation of the upper and lower jaw bone tissue in patients with diabetes mellitus assessed by dental computed tomography. *Actual problems in dentistry*. 2021; 17(2): 148-155. doi: 10.18481/2077-7566-20-17-2-148-155
  33. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C. Pathophysiology of type 2 diabetes mellitus. *Int J Mol Sci*. 2020; 21(17): 6275. doi: 10.3390/ijms21176275
  34. Bunney PE, Zink AN, Holm AA, Billington CJ, Kotz CM. Orexin activation counteracts decreases in nonexercise activity thermogenesis (NEAT) caused by high-fat diet. *Physiol. Behav*. 2017; 176: 139-148. doi: 10.1016/j.physbeh.2017.03.040
  35. Fu Z, Gilbert ER, Liu D. Regulation of insulin synthesis and secretion and pancreatic beta-cell dysfunction in diabetes. *Curr Diabetes Rev*. 2013; 9(1): 25-53.
  36. Halban PA. Proinsulin processing in the regulated and the constitutive secretory pathway. *Diabetologia*. 1994; 2: S65-S72. doi: 10.1007/BF00400828
  37. Boland BB, Rhodes CJ, Grimsby JS. The dynamic plasticity of insulin production in beta-cells. *Mol Metab*. 2017; 6(9): 958-973. doi: 10.1016/j.molmet.2017.04.010
  38. Rorsman P, Ashcroft FM. Pancreatic  $\beta$ -cell electrical activity and insulin secretion: of mice and men. *Physiol Rev*. 2018; 98(1): 117-214. doi: 10.1152/physrev.00008.2017
  39. Seino S, Shibasaki T, Minami K. Dynamics of insulin secretion and the clinical implications for obesity and diabetes. *J Clin Invest*. 2011; 121(6): 2118-2125. doi: 10.1172/JCI45680
  40. Cuinas A, Garcia-Morales V, Vina D, Gil-Longo J, Campos-Toimil M. Activation of PKA and Epac proteins by cyclic AMP depletes intracellular calcium stores and reduces calcium availability for vasoconstriction. *Life Sci*. 2016; 155: 102-109. doi: 10.1016/j.lfs.2016.03.059
  41. Sonal V, Sandeep P, Kapil G, Christine R. Evaluation of condylar morphology using panoramic radiography. *J Adv Clin Res Insights*. 2016; 3(1): 5-8.
  42. Suhartini. Kelainan pada temporo mandibular joint (TMJ). *Stomatognathic J Kedokt Gigi Univ Jember*. 2011; 8(2): 76-85.