REVIEW ARTICLE

The Pathological Effect of Type 2 Diabetes on the Alveolar Bone, Maxilla and Mandible

SHABALINA IRINA MIKHAILOVNA[1], LAPINA NATALIA VIKTOROVNA[2], SKORIKOVA LYUDMILA ANATOLEVNA[3], POPKOV VICTOR LEONIDOVICH[4], NIKOLENKO VLADIMIR NIKOLAEVICH[5], KOCHUROVA EKATERINA VLADIMIROVNA[6], TAUSHANOV DMITRY VLADIMIROVICH[7],

[1]*Postgraduate at the Department of Orthopedic Dentistry, Kuban State Medical University;*
[2]*Doctor of Medical Sciences, Assistant Professor, Head of Department of Orthopedic Dentistry, Kuban State Medical University*
[3,4]*Doctor of Medical Sciences, Professor, Department of Orthopedic Dentistry, Kuban State Medical University*
[5]*Doctor of Medical Sciences, Professor, Head of Department of Human Anatomy, Sechenov First Moscow State Medical University*
[6]*Doctor of Medical Sciences, Professor of Department of Orthopedic Dentistry, Sechenov First Moscow State Medical University*
[7]*Student of dentistry, Kuban State Medical University*
Correspondence to Shabalina Irina Mikhailovna, Email: irinashabalina32@gmail.ru

Urgency: Type 2 Diabetes mellitus (DM) is a systemic metabolic diseasethat results in the pathology of almost all organs and tissues of the human body.Diabetes has proved to be an important risk factor for the development of severe and progressive forms of periodontal tissues damage as well as foot plantar surfaces of teeth damage thatmay subsequently lead to their destruction and loss of tooth-bearing joint.Periodontitis is detected in 100% of patients suffering from Type 2 DM[1-9]. Patients with diabetes also have a high and very high degree of caries according to the CFR index (Caries index, filling, removed) where the percentage of teeth removed[1,3,4,5,7,9] predominates. Factors mentioned above have proved that patients with type 2 DM are in high need of prosthetic dentistry[5,7,9].

Another significant complication of type 2 DM is diabetic osteopathy including osteopenia, osteoporosis, Sharkoarthropathy and diabetic foot syndrome.Negative effect of type 2 DM on the bone tissue affects all skeletal bone structures[10,11]. Therefore, changes in the bone tissue of the periodontium and jaws must be taken into account for qualitative orthopedic dental rehabilitation and replacement of dental defects in patients suffering from type 2 DM.

Aim: To study the effect of type 2 diabetes mellitus (DM) on thebone tissue of the periodontium and jaws according to modern data (2013-2019).

Pathogenesis of Bone Tissue Change under Type 2 DM: Type 2 DMleads to bone tissue microarchitectonics disorder. Modern scientists describesome cases of the development of classical osteoporosis in patients with diabetes, when the development of osteoporosis can be complicated by diabetes (coexistent affection skeleton lesion), as well as the bone tissue damage in patients with uncontrolled diabetes without osteoporosis[12].

Several pathogenetic mechanisms of bone tissue change in patients with type 2 DMhave already been studied nowadays.

One of the most important factors leading to thedecrease in bone strength under type 2 diabetes mellitus is the post-translational glycation of collagen in the bone matrix. Enzymatic crosslinks among collagen molecules provide the strength of the normal bone matrix whilethe collagen matrix activates plasticity thus allowing the bone to withstand deformation without breaking. Persistently high glucose level results in accumulation of advanced glycation end-products (AGEs). In collagen, AGEs cause the formation of non-enzymatic crosslinks thus reducingthe collagen matrix plasticity that in turn results in the bone destruction under deformation.

Constant balance between the bone formation by osteoblasts and its osteoclastic resorption is the key factor to normal quality and quantity of the bone tissue. Under DM type 2 the processes of bone remodeling and bone turnover are disrupted: old bone tissue which has collagen crosslinks due to AGEs will not be renewed that results in bone degradation. Also, AGEs directly affect the cells of bone formation: they suppress mineralization in cell lines of osteoblast precursors; inhibit osteoblastic differentiation by reducing transcription factors; elicit apoptosis of osteoblasts and osteocytes[13,14]. Currently AGEs are believed to play a crucial role in the development of diabetic complications, because hyperglycemia and oxidative stress accelerate the formation of AGEs[13].

According to thestudy, the concentration of amino acid homocysteinein the plasma of patients with type 2 diabetes mellitus increases, which induces osteoblast dysfunction, increases osteocyte apoptosis, promotes accumulation of AGEs, which in its turn reduces bone formation and remodeling and increases the number of AGEs collagen crosslinks.Thus, hypergomocysteinemia can contribute to thereducing of the bone tissue strength under DM type 2[13]).

Adiponectinis supposed to play a great role in bone formation.This protein stimulates osteocalcin expression and differentiation as well as osteoblasts mineralization. Hypoadiponectinemia, which is often seen in obesity and DMtype 2, may be involved in reducing bone strength.

Qualitative and quantitative assessment of the bone tissue is carried out by means of densitometry when bone mineral density (BMD) is determined.The data of the studies concerning BMD underDM type 2 are rather contradictory. In earlier studies it is noted that in type 2DM there is an increase in BMD or this indicator remains within the physiological norm.

Disorders in the bone structure at normal or increased bone mineral density are defined due to changes in the structure of the organic component of bone tissue.In DMtype 2 shows a decrease in sensitive markers of bone formation and resorption, such as osteocalcin and C-terminal cross-linking of collagen, with normal values of other markers of bone metabolism[10]. The following publications have noted the decrease in BMD in individuals with type 2 diabetes. It is described that a more pronounced decrease in BMD was observed in patients

with poorly controlled type 2 DM, and improvement in glycemic status has reduced bone mass loss over a short period of time. Therefore, satisfactory glycemic control can protect patients with type 2 diabetes from bone mass loss[4]. Balajinskaya A.A. et al., 2013, studied the effect of the duration of 2-type DM disease on lumbodorsal spine BMD. Thus, they concluded that in patients with long (more than 12 years) experience of DM type 2, lumbar spine BMD indicators are lower than in patients with experience of disease less than 12 years[15].

Another effect of hyperglycemia is glucosuria, which contributes to hypercalciuria, leading to the mobilization of calcium from the bone depot and the reduction of BMD.Diabetic micro-vascular complications with microcirculation disorders in the bone tissue are one of the causes of bone quality deterioration and increased fragility[11].

A number of studies demonstrate the effect of vitamin D on bone remodeling processes and the course of DMtype 2.Vitamin D deficiency is associated with an increased risk of diabetes due to impaired synthesis and secretion of insulin, and in patients with already established diagnosis of diabetes type 2, a low level of vitamin D increases the risk of development and progression of macro- and microvascular complications.

A review article by Babenko A.Y. et al., 2015, shows that most type 2 DM patients (64%) had vitamin D deficiency[10]. The correlation of vitamin D deficiency with the risk of developing type 2 DM in combination with osteopenia[4] has also been proven.

Against the background of type 2 diabetes, not only the quality of bone tissue deteriorates, but also bone formation decreases: the old bone is replaced more slowly by the new one. Rodent studies also support the hypothesis that regardless of the level of BMD, diabetic bone has reduced mechanical strength. In general, reduced bone formation with reduced bone quality increases the risk of fractures in type 2 diabetes[14].

Elevated glucose level in type 2 DM leads to accumulation of AGEs (Advanced Glycation End Product), hypergomocysteinemia, hypoadiponectinemia, thereby worsening the quality of bone tissue, which is a risk factor for bone fracture.This is confirmed by a study by Farr J.N. et al., 2015, by assessing (in vivo) the strength of bone tissue in type 2 diabetes with the Osteo Probe device – a portable pocket micro-indicator that measures the ability of bone material to resist indentation. According to this study, bone strength in type 2 diabetes is 10% lower compared to the control group. The difference persists after correction for body mass index and correlates with the average value of glycated hemoglobin HbA1c[16].

Effect of DM type 2 on periodontal and alveolar bone: Periodontitis is the most common bone disease and one of the first clinical manifestations of type 2 diabetes. Loss of the alveolar bone is one of the main results of periodontitis, and diabetes is one of the main risk factors for periodontal disease.

Periodontitis is initiated by the invasion of bacteria or their metabolic products into the gingival connective tissue, which initiate the host reaction, which leads to inflammation and loss of the supporting tissues of the tooth[17]. In animal models, diabetes type 2 leads to increased production of tumor necrosis factor (TNF) in the epithelium and connective tissue.

Periodontal infection causes an increase in apoptosis of fibroblasts, epithelial cells and connective tissue, which is significantly enhanced in diabetes. This is important because it is believed that diabetes-enhanced inflammation and apoptosis adversely affects the gums, causing loss of epithelial barrier function and inhibiting recovery processes. All this leads to the loss of gingival junction[18,19].

The pathogenesis of the potential mechanism of bone mass loss in diabetes with respect to osteoblasts and osteoclasts is quite complex. Normally, the process of bone remodeling begins with bone resorption by osteoclasts, followed by the formation of new bone by osteoblasts in resorption lacunae. Altered bone metabolism in diabetes type 2 leads to violation of bone remodeling due to negative effects on osteoclasts and osteoblasts.

Animal studies have shown that diabetes type 2increases the formation of osteoclasts in inflamed areas. In rats with diabetestype 2, there is a 2-4-fold increase in the number of osteoclasts after damage to the dentoalveolar junction by a bacterial pathogen that causes periodontitis, compared to the level of osteoclasts in the control group of rats. A higher degree of inflammation and a more persistent inflammatory response in periodontal disease in DM type 2 rats compared to the control group in response to the same periodontal injury was reported[14].

According to studies in patients with periodontitis and diabetes, the levels of local inflammatory mediators, such as interleukin -1 β (IL-1β), tumor necrosis factor α (TNF-α) and prostaglandin E2, are significantly higher, which leads to longer formation and increased activity of osteoclasts. Patients with type 2 DM and periodontal diseases show elevated levels of TNF-α and IL-6, which are also associated with increased dyslipidemia and lipid peroxidation. Diabetes increases the activity in the ligand receptor system RANK/RANKL/OPG, a key link of bone homeostasis that directly regulates the differentiation of osteoclasts and osteolysis[14].

The alveolar bone of rats with diabetes mellitus has been studied by Yilmaz Nezih et al (2018). In a comparison with the control group, rats with diabetes are shown a disorganization and degeneration of periodontal fibers with loss of attachment of Charpy fibers. Enlarged resorbative regions on both surface of cement and alveolar bone, were evident as an addition to changes in the architectonics of bone trabecules[20]. The same results were obtained in the study ofMedhat Ahmed El-Zainy et al[21].

Reactive oxygen species (ROS) are known to be one of the causes of diabetes-related periodontitis. Invasion of bacteria into the periodontium starts the release of inflammatory cytokines and leads to the increase in the number and activity of neutrophils that excrete ROS in periodontitis. During the bone resorption, osteoclasts containing NADF oxidase produce superoxideactively. Simultaneously, neutrophils in diabetic patients produce more superoxide than neutrophils from normal elements. The imbalance between ROS production and antioxidant protection leads to the increasing of oxidative stress. Some ROS (such as superoxide and hydrogen peroxide) activate osteoclasts and accelerate their formation[14].

There is evidence that both diabetes and bacterial infection in periodontitis enforce osteoblasts cell apoptosis, thereby reducing bone communication. Sandra Pacios (2013), in the research of diabetic-induced rats performed that bacterial infection doubled the number of cells expressing TNF and increased the number of apoptotic cells adjacent to bone by a factor of 10[22].

DM also increases the loss of periodontal ligament cells. It is induced by periodontal infection by means of increasing apoptosis of these cells. This loss is significant because the periodontal ligament is a rich in protein source that are able to differentiate into osteoblasts[7].

It is revealed that increased alveolar bone loss caused by bacterial infection in diabetic patients is accompanied by increased receptor expression for end-products of extendedglycation (RAGE) in gum tissue. That prevents osteoblast differentiation and induces their apoptosis. Elevated levels of AGEs are found in diabetic periodontal, and AGE-RAGE interaction leads to increased expression of pro-inflammatory cytokines and induces osteoblast apoptosis[7].

Thus, diabetes prolongs inflammation and osteoclastogenesis in periodontitis and by means of TNF limits the normal repair process by negatively modulating the factors that regulate bone tissue synthesis[23].

The research (Liu R et al., 2006) is proved the above described effects of influence of 2 type DM on a periodontium and an alveolar bone: persistent inflammatory reaction in a periodontium, violation of a periodontal ligament and resorption of an alveolar bone by means of increasing in number and activity of osteoclast and deterioration in formation of a new bone tissue because of strengthening of apoptosis of osteoblasts and fibroblast[24].

In the research of Mohamed Alasqa (2018), periodontal parameters were rated in patients against the background of DMtype 2, prediabet and somatically healthy people: periodontal parameters were worse in patients with prediabetes and DM type 2 than in the control group, but these parameters were compared between prediabet and DM type 2 patients[25].

Jung-Sun Moon (2019), studying in vivo in rats the influence of mechanical impact on parodont tissues against the background of DM 2 type, made a conclusion that the additional mechanical overload of teethaggravates synergy the course of a periodontal disease, and it can lead to an accidental blasting resorption as well as to the frontal resorption of an alveolar bone of an osteoklastama. Reducing tooth overload and controlling the level of final glycation products may prove to be a good therapeutic agent for diabetes-induced alveolar bone destructiontreatment[26]. These observations are indirectly proved in the work of Chuev V.P. et al., 2017. The research studies the effect of prosthetics on the condition of alveolar bone in patients with DMtype 2. The patients with dental defects, the remaining teeth probe increased chewing stress that makes conditions for the destruction of the closing cortical plate. In patients suffering from DMtype 2, 3 years after the application of bridge prostheses, the X-ray pattern in the area of the support teeth is much better and the optical density of the jaws increased, although it remains less of age-appropriate normal value[18,19].

Leading X-ray signs of periodontitis against background of DM type 2 are disappearance of cortical plate, presence of various destructive changes in bone tissue of alveolar process[27].

Generalized horizontal and localized vertical loss of alveolar bone[28,29,30] is distinctive. A number of researchers believe that in the presence of periodontopathy in patients with type 2 DM, a specific funnel-like type of bone resorption of the alveolar process is formed. It is noted that such clinical-radiological pattern of periodontitis is observed only in diabetic patients with traumatic dental overload, as well as in those patients who are not following a diet and not receiving systematic anti-diabetic treatment[31].

The risk and extent of alveolar bone loss is positively correlated with the lack of metabolic control in patients suffering from DM type 2[17]. Tanous S, Joshi B.C., 2018, concluded that early therapeutic intervention and control of glucose level as well as HBA1c level in patients with DM type 2 can be reversed up to the restoration of alveolar bone defect against the background of the loss of bone mass of the alveolar process without any organic matrix disorders[32].

Thus, diabetes mellitus and periodontal diseases are closely related. Permanent hyperglycemia leading to increased immune-inflammatory reactions induced by periodontal pathogens results in severe periodontal diseases in patients suffering from DMtype 2.

Condition of bone tissue of upper and lower jaw against the background of DM type 2: Bone tissue of jaw is inhomogeneous in its form and structure. The lower jaw is represented by a thicker cortical and denser trabecular (spongy) bone in comparison with the upper jaw. At the same time, the trabecular bone in the distal sections of both jaws reveals lower density and thickness. The study performed by Dutmanee Seriwatanachai et al, 2015[33] provides more information concerning the density and structure of bone tissue of jaw. The densitometry of the jaws carried out by means of cone-beam computed tomography (CBCT) demonstrated thatthat the area of highest density is located in the frontal part of the lower jaw with the further decrease in the following order: the frontal part of the upper jaw, the distal part of the upper jaw, the distal part of the lower jaw. The density of cortical and trabecular bone in the regions of different tooth groups was also measured. The lowest density of the cortical bone tissue was recorded on the vestibular surface of the lower incisors, while the highest density was on the retromolar region of the lower jaw.

Using the Mish X-ray scale (2008) to determine bone tissue qualities, it was revealed that the cortical bone of the upper jaw of the highest density were localized in the regions of fangs and molars, whereas the upper incisors and premolars demonstrated the similar density range. Notably, the retromolar surface of the upper jaw was classified only in accordance with the type III or IV of the Mish scale, which proposed that significant lack of stability for implants installed in this area. In addition, the density of the spongy bone of the upper jaw is comparable to that of the lower jaw in the region of incisors, premolars, and molars, with the exception of the retromolar region and the region of fangs, which possess the lowest density of the spongy bone in comparison to all regions of the upper jaw.

A. Nemtoi et al., 2013, in their study in the structure of mandibular bone tissue of lower jaw (performed in accordance with the cone-beam computed tomography method) before the implantation revealed an evident correlation between the patient's gender, age and bone type. In most women patients, the bone density of the second type in accordance with the Mish scale, while in male patients the prevalent ones were types II and III. With the increase in age of examined patients the prevalence of type IV of the bone tissue of jaw was detected[34].

Most studies devoted to the structure and density of bone tissue of jaws in patients suffering from DM type 2 indicate the changes in the latter against the background of somatic diseases.

Saadettin Kayipmaz et al., 2017, examined the state of the bone tissue of the lower jaw in 23 patients with DM type 2 and 23 patients not suffering from diabetes[35] by means of the CRCT method. No statistically significant differences in radiomorphometric measurements and fractal dimension analysis were revealed between the group of patients with DM type 2 and the control group. The quantitative evaluation of the mandibular bone revealed the thinning of the cortical bone with a statistically significant difference between patients with DM type 2 and healthy patients of the control group.

Kazuo Onoyama et al., 2011, studied the state of mandibular bone tissue in patients with DM type 2 and somatically healthy people; both groups of patients were comparable in age and gender[28]. The alveolar ridge level did not significantly differ in the group of patients with DM type 2 and the control group. In patients with DM, the density of the trabecular bone of the jaw was significantly reduced in comparison with the control group, but there was no significant difference in cortical bone density. The indices of morphological changes and stress/strain index as well as the criteria of bone strength were significantly reduced in patients with DM type 2 in comparison with those of patients without diabetes. The morphometric indices revealed a rougher structure of the trabecular bone in the diabetic group in comparison with the control group. This study demonstrated that the diabetic condition expressed the evident influence on the trabecular bone of the lower jaw resulting in the decrease of its qualities.

The group of researchers also revealed the decrease in BMD of spongy jaw bone in patients with diabetes mellitus type 2 in comparison with the somatically healthy people, comparable in age and gender[13,36,37].

A. Nemtoi et al., 2013, examined the lower jaws in 23 DM type 2 patients and 27 control patients by means of CRCT. The distance from the mandibular canal to the alveolar process as well as the distance between the buccal and lingual cortical walls of the lower jaw were measured. In addition, bone quality was evaluated by measuring BMD. There was a significant inverse correlation between cortical and trabecular bone density in the distal mandible and HbA1c level. This result demonstrated that the low bone density level (34) was detected at high HbA1c levels.

This correlation is proved by the study performed by M. Lobna. In addition, the authors highlighted the osteoporetic changes in bone tissue of jaws in patients with DM type 2[39].

Thus, the importance of maintaining good metabolic control in patients with DM type 2 was proved within the prevention of osteoporotic changes.

JayarekhaTadiparthi, 2016, examining the toothless jaws of patients with DM type 2 by means of the digital orthopantomography concluded that in patients suffering from DM the residual resorption of the alveolar process significantly predominates in the areas of premolars of the upper and lower jaw and those of the angle of the lower jaw. It was also found out that the degree of residual bone resorption in patients suffering from DM was influenced rather by the increased HbA1C than by the time limitation of tooth loss[39].

According to the studies of A.V. Skiba and T.P. Tereshina, 2014, 60.3% of patients with DM type 2 have destructive changes in bone, while 26.2% suffer from the dystrophic sclerotic displacement[7].

Jolly SJ, Hegde C, Shetty NS., 2015, compared BMD in non-diabetic patients and in examined patients suffering from diabetes mellitus type II by means of the spiral digital tomography. The study was performed on the group of 40 toothless men including 20 healthy persons as well as 20 patients suffering from DM type II aged 50 to 65. Glycemic control of diabetic patients was estimated by the level of glycolized hemoglobin. The diabetic control group had HbA1c level between 6.1 – 8. The density values of trabecular and cortical bone tissue of the upper and lower jaw revealed no significant differences between patients with DM type 2 and healthy patients. Within the limits of this study it is possible to conclude that the bone density in the examined patients with DM type II seems not to change[40].

CONCLUSION

Nowadays, many foreign references describe the changes in bone tissue of periodontium and jaws against the background of DM type 2 as well as the differences between topographic areas of jaws; the correlation of these changes to the gender is also revealed. The evident dependence of a damage degree of jaw bone tissue and periodontal tissue upon the level of metabolic control was also revealed. These data allow experiencing the more detailed and qualitative planning of replacement of defected dentitions in patients suffering from DM type 2 and also increasing the service cycle of artificial orthopedic structures. At the same time, the dependence of changes in bone tissue of upper and lower jaw in patients suffering from DM upon the age of the patient, duration of the disease, length of defected dentition as well as presence of specific changes in bone structures of maxillar and mandibular joint are not sufficiently studied.

REFERENCES

1. Gileva, O.S. Features of diagnosis and treatment of xerostomicsyndrome in periodontal diseases and mucous membrane epithelium of the mouth in patients with diabetestype 2 /O.S. Gileva, E.N. Smirnova, A.A. Pozdnyakov, T.V. Libik//Russian Medical Journal. - 2016. - N. 20. - P.1340-1345.
2. Juraeva, S.F. Clinical and epidemiological characteristics of inflammatory and destructive lesions of periodontal tissues in patients with impaired glucose homeostasis / S.F. Juraeva,

M.V. Vorobyov // Practical Medicine. - 2016. - № 8 (100). - P. 104-106.
3. Iordanishvili A.K. Features of pathology of hard teeth tissues in adults with diabetes type 2 / A.K. Iordanishvili, E.A. Khromova, N.A. Udaltsova, T.V. Volkova // Institute of Dentistry. - 2016. - № 3 (72). - P. 32-35.
4. . Iordanishvili A.K. Analysis of the prevalence rate of periodontal tissue diseases in adults with diabetestype 2 /A.K. Iordanishvili, E.A. Khromova, N.A. Udaltsova, T.V. Volkova, O.V. Prisyazhnyuk//Institute of Dentistry. - 2016. - № 4.- P.18-20.
5. Novitskaya I.K. Prevalence rate and intensity of dental pathology in patients with diabetes/I. K. Novitskaya, T. P. Tereshina, T. I. Dimcheva, A. A. Babenya, N. V. Mozgovaya//Innovations in dentistry. - 2014. - № 1.- P. 11-13.
6. Prozorova, N.V. To assess the state of the oral cavity in patients with diabetes / N.V. Prozorova, K.E. Mamykin, R.A. Fadeev // Institute of Dentistry. - 2015.- № 4.- P.69-69
7. Skiba A.V. Diabetes and periodontal diseases/A.V. Skiba, T. P. Tereshina//Innovations in dentistry. - 2014. - № 1. - P. 51-57.
8. Skiba A.V. Oral tissues conditionin patients with diabetes type 2 / O.V. Skiba, A. E. Denga, V.Ya. Skiba // Innovations in dentistry - 2017. - N. 1.
9. Khanov I.A. Study of dental health in patients with diabetestype 2 /I.A. Khanov, M.A. Schumchenko, I.Z. Zabezhinskaya, K.V. Saburova//"Interdisciplinary approach to diagnosis, treatment and prevention of periodontal tissue diseases in patients with diabetes". Under editorship of N.A. Udaltsova, M.A. Okuneva. Conference information package. – St.P.: St. Petersburg, 2018. -P.61-63.
10. Babenko A.Y. Diabetes and Bone / A.Y. Babenko, V.S. Nikitin, T.L. Karonova // Medical Council. - 2015. - № 17. - P.108-113.
11. Mistyakov M.V. Diabetes and osteoporosis/M.V. Mistyakov, T.V. Bardymova, S.S. Tsyretorova//Siberian Medical Journal (Irkutsk).- 2015. № 6.- P.47-52.
12. Yalochkina T.O. Lowtrauma fractures and bone remodeling in diabetestype 2 /T.O. Yalochkina, Zh.E. Belaya//Obesity and metabolism. - 2017. - № 14 (3).- P. 11-18.
13. Nurullina, G.M. Features of bone metabolism in diabetes / G.M. Nurullina, G.I. Akhmadullina // Osteoporosis and osteopathy. - 2017. - № 20 (3).- P. 82-89.
14. Ying-Ying Wu. Diabetes mellitus related bone metabolism and periodontal disease / Ying-Ying Wu, E Xiao, Dana T Graves // International Journal of Oral Science. – 2015. – Vol. 7(2). - P. 63–72.
15. Balazhinskaya, A.A. Features of bone mineral density in patients with type 2 diabetes / A.A.Balazhinskaya, G.N. Romanov, V.A. Domantsevich// Problems of Health and Ecology. - 2013. - №3 (37).–P. 77-82.
16. Farr JN. Determinants of bone strength and quality in diabetes mellitus in humans. Bone / Farr JN, Khosla S // 2016. – Vol.82. – P. 28-34.
17. Xiao E. Impact of Diabetes on Periodontal Disease / Xiao E., Wu Y., Graves D.T. // In: Lecka-Czernik B., Fowlkes J. (eds) Diabetic Bone Disease. Springer, Cham. – 2016.- P. 95-112.
18. Asadov R.I. Dynamics of optical density of periodontal bony tissue in the area of abutment teeth in women with type II diabetes/R.I. Asadov, V.D. Dorokhova//Institute of Dentistry. - 2017.- № 4.- P.41-43.
19. Chuev V.P. Dynamics of optical density of bone tissue in men suffering from diabetes type 2 in the area of abutment teeth of dental bridges / V.P. Chuev, R.I. Asadov, A.A. Kopytov, A.V. Tsimbalistov // Institute of Dentistry. - 2017. - № 4.- P. 41-43.
20. NezihYilmaz. Effects on alveolar bone of diabetes mellitus induced by Streptozotocin in rats. Histopathologic and immunohistochemical study / NezihYilmaz, Ibrahim Uysal, VeyselEratilla, IrtegünSevgi// International Journal of Morphology. – 2018. – Vol. 36 (1). – P. 206-211.
21. Medhat Ahmed El-Zainy. Effect of diabetes mellitus on cementum periodontal interface in Streptozotocin-induced diabetic rat model / Medhat Ahmed El-Zainy, Ahmed Mahmoud Halawa, Fatma Adel Saad // Future Dental Journal. – 2018. – Vol. 4, № 2. – P. 181-188.
22. Sandra Pacios. Bacterial Infection Increases Periodontal Bone Loss in Diabetic Rats through Enhanced Apoptosis / Sandra Pacios, OelisoaAndriankaja, Jun Kang, Maher Alnammary at al. // The American Journal of Pathology. – 2013. - Vol. 183, №6, P. 1928-1935.
23. Sandra Pacios. Diabetes aggravates periodontitis by limiting repair through enhanced inflammation / Sandra Pacios, Jun Kang, Johnah Galicia, Kenneth Gluck // The FASEB Journal. – 2012. – Vol.26 (4), P. 1423–1430.
24. Liu R. Diabetes enhances periodontal bone loss through enhanced resorption and diminished bone formation / Liu R, Bal HS, Desta T, Krothapalli N at al. // Journal of Dental Research. – 2006. – Vol. 85, № 6. - P. 510-514.
25. Mohammed Alasqah. Periodontal parameters in prediabetes, type 2 diabetes mellitus, and non-diabetic patients / Mohammed Alasqah , Sameer Mokeem, Ali Alrahlah, Nawwaf Al-Hamoudi // Brazilian Oral Research. - 2018. - Vol.32
26. Jung Sun Moon. Synergistic alveolar bone resorption by diabetic advanced glycation end products and mechanical forces / Jung Sun Moon ,Su Young Lee, Jung Ha Kim, Yoon Ho Choi // Journal of Periodontoiogy.-2019.-Vol. 90, № 12. – P. 1457-1469.
27. SafarovaS.S. Bone remodeling in type I diabetes/S.S. Safarova//Bulletin of Siberian medicine. - 2018. - № 17 (3).- P. 115- 121.
28. Lidya I. Nainggolan. Prevalence of alveolar bone deffect pattern in periodontitis patients with diabetes mellitus using bitewing radiography / Lidya I. Nainggolan, LavaneyaGunasagaran // Journal of Dentomaxillofacial Science. – 2018. – Vol. 3, №2. – P. 88-90.
29. Kazuo Onoyama. Comparison of mandibular trabecular structures between normal and diabetic rats: evaluation of spontaneous type 2 diabetes in a rat model / Kazuo Onoyama,YusukeKozai, RyotaKawamata, Takashi Sakurai // Oral Radiology. – 2011. – Vol. 27, №1. - P. 35-42.
30. Sarah K. Sonnenschein. Generalized severe periodontitis and periodontal abscess in type 2 diabetes: a case report / Sarah K. Sonnenschein // Balkan Journal of Dental Medicine. – 2016. – Vol. 20, №2. - P. 111-116.
31. Polushkina N.A. Condition analysis of bone tissue of the upper and lower jaws in patients with diabetes/N.A. Polushkina, N.V. Chirkova, J.V. Vecherkina, T.V. Zubkova// Tendency in the development of science and education. - 2017. - № 28-2.- P. 27-29.
32. Tanous S. Case report: effect of blood glucose/A1c on periodontal/alveolar bone health / Tanous S., Joshi BC // Journal of Dental Health, Oral Disorders & Therapy. - 2018. – Vol. 9(2). – P. 186–187.
33. DutmaneeSeriwatanachai. Reference and Techniques used in Alveolar Bone Classification / DutmaneeSeriwatanachai, SirichaiKiattavorncharoen, NawakamonSuriyan, KiatanantBoonsiriseth at al. // Journal of Interdisciplinary Medicine and Dental Science. – 2015. - Volume 3, №2.
34. Nemtoi A. Quantitative and qualitative bone assessment of the posterior mandible in patients with diabetes mellitus: a cone beam computed tomography study / Nemtoi A, Ladunca O, Dragan E, Budacu C at al. // Revista medico-chirurgicala a Societatii de Medici siNaturalistidin Iasi. – 2013. – Vol.117, №4. -P. 1002-1008.
35. SaadettinKayipmaz. Osteoporotic mandibular changes caused by type 2 diabetes mellitus: a comparative study by cone beam computed tomography imaging /

SaadettinKayipmaz, Ömer Said Sezgin, SalihaAkçay // Oral Radiology. – 2017. – Vol. 33, №2. -P. 108-116.
36. Anju P David. Assessment of panoramic radiomorphometric indices of mandible in diabetes mellitus patients and non diabetic individuals / Anju P David,BeenaVarma, SeemaKurup, Dhanya Mary Sam at al // Journal of Clinical and Diagnostic Research. - 2017. - Vol.11, №11. -P. 35-39.
37. Zhang W. Cone Beam Computed Tomography of mandibular bone density in non-diabetic vs. diabetic populations / Zhang W, Al Hatem O, Edwards L, Wang BY. // Texas Dental Journal. – 2016. - № 133 (7). -P. 414-422
38. Lobna M. El Saadawy. Relation of cone beam computed tomography assessment of mandibular bone density to dual energy X-RAY absorptiometry in type 2 diabetes mellitus patients / Lobna M. El Saadawy,Rania A. Fahmy, Khaled A. Matrawy, Mohammed H. Zeitoun at al. // Alexandria Dental Journal. – 2019. - Vol.44. - P. 87-92.
39. JayarekhaTadiparthi. Evaluation of vertical bone heights of maxillary and mandibular residual ridges among edentulous diabetics by digital orthopantomograph / JayarekhaTadiparthi, Sujatha D. // International Journal of Current Research. – 2016. - Vol.8, № 10. -P. 40608-40612.
40. Jolly SJ. Assessment of Maxillary and Mandibular Bone Density in Controlled Type II Diabetes: A Computed Tomography Study / Jolly SJ, Hegde C, Shetty NS. // Journal of Oral Implantolgy. – 2015. – Vol. 41, №4. - P. 400-405.