Vitamin D deficiency in obese children.

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Abstract: Vitamin D deficiency is prevalent in childhood obesity. Excess adiposity is linked with poor vitamin D status, and the effects of this deficiency during obesity appear to have several health implications, including IR, inflammation, and compromised bone growth/mineralization.

Keywords: health implications, including IR, inflammation, and compromised bone growth/mineralization.

In addition, since vitamin D is fat-soluble, people with higher amounts of body fat will 'sequester' vitamin D in fat cells, leading to lower amounts circulating in the blood. Due to this, people with obesity typically need higher amounts of vitamin D to maintain adequate levels and/or to correct a deficiency.

Vitamin D deficiency and childhood obesity have been classified as epidemics throughout the world, and both share some common risk factors including poor diet and inactivity. Observational and clinical studies show that vitamin D status and fat mass are inversely correlated. It is not clear whether vitamin D deficiency contributes to, or is a consequence of obesity, or whether there are regulatory interactions between excess adiposity and vitamin D activity. The effects of this deficiency in childhood obesity appear to have negative influences on overall health, including insulin resistance, inflammation, and impeded bone mineralization, as well as increased future risk of type 2 diabetes, cardiovascular disease, and osteoporosis. The rather ubiquitous distribution of the vitamin D receptor and the 25-hydroxyvitamin D 1a-hydroxylase throughout the body, including evidence for a role of vitamin D in adipogenesis and adipocyte metabolism, may in part explain these widespread effects. Most of the findings to date suggest that the vitamin D needs of obese children are greater than the nonobese. Although ultraviolet B-induced skin synthesis is a main source of vitamin D, its use is neither feasible nor prudent due to limited sun availability for many and concerns for skin cancer. Likewise, obtaining adequate vitamin D from natural food sources alone is generally not achievable, and even in countries that allow fortification, vitamin D intakes are low. Therefore, in obese children, vitamin D supplementation is warranted. Weight loss interventions using energy restriction and physical activity may also improve the poor vitamin D status associated with obesity. More research is needed to define optimal vitamin D status in this vulnerable population, including investigations to determine the efficacy of vitamin D supplementation in attenuating the conditions

associated with childhood obesity, and to further elucidate the mechanisms by which vitamin D exerts its effects on health.

Although classified as a nutrient (largely due to the timing of its discovery which coincided with the discovery of other fat-soluble vitamins), vitamin D is more fittingly described as a prohormone/hormone.9 It exists in two forms: vitamin D2 and vitamin D3. Vitamin D2, or ergocalciferol, is a photoproduct of the irradiation of ergosterol, a fungal sterol also known as provitamin D2. Vitamin D3, or cholecalciferol, is produced following the irradiation of provitamin D3 (7-dehydrocholestrol) in the epidermis and dermis layers of the skin.10 The term "vitamin D" without a subscript refers to vitamin D2, vitamin D3, or both. The primary source of vitamin D is from skin synthesis as there are few naturally occurring dietary sources.

Both vitamin D2 and vitamin D3 are hydroxylated twice to become active and capable of binding to their vitamin D receptor (VDR). The first hydroxylation occurs in the liver via 25-hydroxylase, forming 25-hydroxyvitamin D (25(OH)D) (also known as calcidiol). This is the major circulating form of vitamin D and is the primary determinant of vitamin D status. The enzyme 25-hydroxyvitamin D 1α-hydroxylase (1α-OH-ase) converts 25(OH)D to its active form, 1,25-dihydroxyvitamin D (1,25(OH)2D, also known as calcitriol). Although this enzyme is classically identified in the proximal tubules of the kidney, 1α-OH-ase (CYP27B1) gene expression has been demonstrated in a wide range of extrarenal tissues, including, but not limited to, immune, brain, pancreatic, and adipose tissue.12,13 Renal activation of 25(OH)D results in elevated levels of circulating 1,25(OH)2D, which subsequently binds to the VDR in target tissues. Extrarenal formation of 1,25(OH)2D appears to act locally by binding to VDR present within the same or neighboring cells. These intracrine and autocrine/paracrine actions are thought to be regulated by cytokines and to be responsible for the effects of 1,25(OH)2D on cell proliferation, differentiation, and apoptosis.

Vitamin D and its metabolites are transported bound to and solubilized by plasma protein carriers. Vitamin D-binding protein (DBP), a protein primarily produced by hepatic parenchymal cells, is the major transport protein. It binds 85% of circulating 25(OH)D, while albumin and lipoproteins account for the remaining 15%.Once synthesized, from renal or local production, 1,25(OH)2D is transported to nuclear VDR in target cells.16 The human VDR plays a central role in the biological actions of vitamin D as it regulates the expression of numerous genes in a largely ligand-dependent manner.16 VDRs, upon activation by 1,25(OH)2D, form a heterodimer with retinoid X receptors (RXRs). These VDR–RXR heterodimers bind to vitamin D response elements of multiple genes, which results in either the transactivation or repression of these genes.

Throughout childhood, vitamin D plays important roles in calcium and phosphorus homeostasis and bone growth/mineralization. Vitamin D deficiency in childhood causes osteomalacia, leading to growth retardation and skeletal deformities (ie, rickets). More common, however, is an insidious presentation of vitamin D deficiency, which may prevent children and adolescents from reaching peak bone mass and predicted height.

There is evidence that vitamin D is necessary for many other cellular processes. In addition to the organs responsible for calcium/phosphate homeostasis, VDRs are expressed in a variety of tissues and cells such as the hepatocytes, myocytes, adipocytes, pancreatic β-cells, and several immune cells, all of which are associated with obesity and its associated metabolic complications.

Vitamin D deficiency: reemergence, diagnosis, and prevalence in children.

Rickets, first documented in approximately AD by Sorano of Ephesus, is the most recognized disease of vitamin D deficiency as it has plagued humans throughout history. It became especially problematic in Europe and North America during the Industrial Revolution with the related reduction in sun exposure for those living and working in urban environments. Advancements in the science of vitamin D in the mid-20th century led to public health initiatives such as food fortification, which eliminated rickets as a significant health problem in the countries that implemented them. However, in the last 10–15 years, evidence has surfaced for a reemergence of rickets in certain ethnic and minority groups in Europe and Australasia and an alarming prevalence of poor vitamin D status worldwide.The factors speculated to contribute to this rise in vitamin D deficiency include lower intakes of vitamin D-fortified foods, use of sunscreens/blocks, reduced time spent in outdoor activities, and air pollution. Moreover, our understanding of the role of vitamin D in human health has expanded into areas beyond bone and has subsequently put into question the definition of adequate vitamin D status.

Diagnostic criteria.The best available indicator of vitamin D status is the serum concentration of (OH)D,25 although the extent to which this measurement relates to or serves as a predictor of health outcomes has not been fully elucidated. Furthermore, there is no general agreement on the required serum 25(OH)D for adequate status. For example, the Institute of Medicine (IOM) defines vitamin D deficiency, or hypovitaminosis D, as a serum (OH)D concentration <50 nmol/L (20 ng/mL),whereas the Endocrine Society has suggested that a 25(OH)D concentration between 75 nmol/L and 250 nmol/L (30–100 ng/mL) is required for sufficiency, with the intermediate concentration range of 52–72 nmol/L (21–29 ng/mL) classified as “insufficient”.Vitamin D status classifications within pediatric clinical practice guidelines are similarly controversial. The American Academy of Pediatrics

(AAP)28 cut-off values are identical to IOM with a 25(OH)D concentration >50.0 nmol/L considered to be “sufficient”, while the Society for Adolescent Health and Medicine (SAHM)29 considers a 25(OH)D serum concentration between 75–125 nmol/L (30–50 ng/mL) to be “sufficient” for the adolescent.IR and inflammation are commonly seen in overweight/obese children and are predictive of the development of metabolic syndrome, type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), and perhaps osteopenia/osteoporosis. For example, reports indicate that children with these two risk factors are significantly more likely to have T2DM and CVD 25–30 years later compared with their peers.

The relationship between poor vitamin D status and IR, T2DM, and metabolic syndrome is the most well studied and was first observed in obese adults.Similar observations have since been made in obese children. Most, although not all, show significant associations between circulating 25(OH)D concentration and indices of IR and blood glucose control; their findings have been covered in detail elsewhere.The very few published intervention trials using vitamin D supplementation to improve IR and impaired glucose tolerance in obese children or adolescents have yielded beneficial effects. For example, results from our 6-month randomized controlled trial (RCT) of obese adolescents (age =14.1±2.8 years; BMI =39.8±6.1 kg/m2) supplemented with 4,000 IU per day showed an attenuation of IR similar to results involving the use of the drug metformin.By comparison, the results of a 2012 meta-analysis of the evidence on vitamin D supplementation and glycemic control in adults revealed a weak effect of vitamin D supplementation in reducing fasting glucose and improving IR in patients with T2DM or impaired glucose tolerance.Much of this discrepancy can be attributed to differences in methods employed, such as vitamin D dose and outcome measures, and participant characteristics, most notably body weight/fat status, initial vitamin D status, and age. Further, it is speculated that the status of both vitamin D and parathyroid hormone (PTH) needs to be considered in evaluating the impact of vitamin D status on glucose metabolism.More RCTs are warranted.The biological mechanisms by which vitamin D influences glycemic control in obesity have yet to be determined but are thought to involve enhancement of peripheral/hepatic uptake of glucose, attenuation of inflammation, and/or regulation of insulin synthesis/secretion by pancreatic β-cells Moreover, data from one of the first reports to examine the association between vitamin D deficiency and IR in obese children indicated that the most clinically meaningful threshold of serum 25(OH)D concentration for the identification of IR and impaired glucose homeostasis in the obese is 50 nmol/L (20 ng/mL).This is the cut-off used by the IOM in the definition of vitamin D deficiency.

A new systematic review of 35 studies evaluated the degree to which vitamin D and CVD risk factors are associated in obese children.The cross-sectional studies

included in the analysis showed a relationship between (OH)D and systolic blood pressure but not the prospective studies. The lone RCT in the review suggested a relationship between vitamin D status and arterial stiffness. There were no associations between 25(OH)D and diastolic blood pressure or low-density lipoprotein cholesterol, and the links with high-density lipoprotein cholesterol and triglycerides were capricious.

Anther condition related to childhood obesity and metabolic disturbances is nonalcoholic fatty liver disease (NAFLD). Since both NAFLD and serum 25(OH)D concentration are associated with adiposity and IR, interest in examining their potential pathogenic link has emerged. Pediatric NAFLD is a condition characterized by hepatic fat infiltration >5% hepatocytes, as assessed by liver biopsy, in the absence of viral, autoimmune, and drug-/alcohol-induced liver disease. It is becoming one of the most common complications of childhood obesity and is strongly associated with the clinical features of IR, especially the metabolic syndrome and T2DM.Two separate observational studies showed that compared with non-NAFLD obese children and teens, those with NAFLD had significantly lower serum concentrations of 25(OH)D, which was correlated with IR in those with NAFLD but not in those without NAFLD. Another investigation showed that lower 25(OH)D concentration is associated with NAFLD, independent of adiposity, physical activity, and IR.At odds with these findings, an earlier report using data on 1,630 children, aged 12–19 years, from the National Health and Examination Survey (NHANES) 2001–2004, found vitamin D status not to be independently associated with NAFLD. It remains to be determined whether poor vitamin D status contributes directly to the risk of developing NAFLD or if this association is confounded by hepatosteatosis,48 as the liver is a primary site of vitamin D activation.

The bone mass attained during growth is a critical determinant of the risk of osteoporosis later in life. Those with higher peak bone mass after adolescence have a protective advantage during normal aging and menopause when significant bone loss occurs. Although it is known that peak bone mass is determined by genetics and lifestyle factors, the effects of obesity on bone mineral accretion are not fully discerned. In contrast with adults in whom overweight/obesity is protective to bones, there is evidence that obesity in children is a risk factor for low bone mass and fractures.However, this phenomenon is not uniformly observed.Efforts of new investigations have focused on addressing the reasons for the discrepancy, including distribution of body fat (abdominal obesity),and/or the presence of comorbidities, such as IR, metabolic syndrome,and NAFLD.Factors thought to be responsible for the altered bone mass described in childhood obesity include changes in the hormonal milieu (eg, increased conversion of androstenedione to estrogen),and the

participation of adipokines (resistin, adiponectin, leptin, osteocalcin)60 and adipose-derived inflammatory markers (interleukin-6 [IL-6] and tumor necrosis factor-α [TNF-α]) in bone remodeling. Another likely contributor is the poor vitamin D status related to obesity, via its indirect (inflammation) and/or direct (calcium homeostasis/bone mineralization) skeletal effects.

Children have high demands for dietary calcium to support the mineralization of growing bone. It is well established that serum PTH concentration varies inversely with absorbed calcium and serum 25(OH)D concentration. It has been proposed that the point along the 25(OH)D continuum at which PTH becomes constant is an indication of the point at which calcium absorption becomes constant.62 A study of young, healthy children in Canada demonstrated that a 25(OH)D concentration of 100 nmol/L was required to see a plateau in PTH.

Literature:

1. .D. Z, Z., Zh. B, E., & Z. Z, M. (2022). Changes visual systems at patients with essential arterial hypertension. central asian journal of medical and natural sciences, 3(3), 744-750. retrieved from https://cajmns.centralasianstudies.org/index.php/CAJMNS/article/view/85113
2. .Z. , Z. D., & K., M. D. (2022). Magnetic Resonance Tractographyas a Method of Choice for Neuroimaging in Ocular Ischemic Syndrome against the Background of hypertension. central asian journal of medical and natural sciences, 3(2), 207-210. https://doi.org/10.17605/OSF.IO/E2AH912
3. .Zuhriddinovna Z. D., Kamaljanovna M. D. development of classification criteria for neuroretinal ischemia in hypertension //web of scientist: international scientific research journal. –2022. –т. 3. –no. 02. –c. 972-978. https://wos.academiascience.org/index.php/wos/article/view/951/8825
4. .Zuxridinovna, J. D. (2022). Ultrasonic Dopplerography of retinal vessels in acute cerebral ischemia against the background of arterial hypertension. central asian journal of medical and natural sciences, 3(3), 100-106. retrieved from https://cajmns.centralasianstudies.org/index.php/CAJMNS/article/view/73714
5. A Sidikov, D Zaslavsky, A Sadykov, N Ibragimova,M Megna, O Olisova, D Kozlova, R Nasyrov, E. Shalaeva,T Garcia The new differential diagnostic test for the lichenoid drug eruption Dermatologic therapy, 2020 https://doi.org/10.1111/dth.13784
6. Abdurakhmanovich, K. O., & ugli, G. S. O. (2022). Ultrasonic Diagnosis Methods for Choledocholithiasis. Central Asian Journal Of Medical And Natural Sciences, 3(2), 43-47.
7. Abdurakhmanovich, K. O., & ugli, G. S. O. (2022). Ultrasound Diagnosis of the Norm and Diseases of the Cervix. Central Asian Journal Of Medical And Natural Sciences, 3(2), 58-63.
8. Akhmedova Shakhnoza Ozodjonovna. (2023). climate change: everyone's struggle for survival. conference zone, 70–78. retrieved from http://conferencezone.org/index.php/cz/article/view/936
9. Akhmedova Shakhnoza Ozodjonovna. (2023). global implications of climate change. conference zone, 79–86. retrieved from http://conferencezone.org/index.php/cz/article/view/937

10. Akhmedova Shakhnoza Ozodjonovna. (2023). principles of environmental impact assessment. conference zone, 95–107. retrieved from http://conferencezone.org/index.php/cz/article/view/939
11. Akhmedova Shakhnoza Ozodjonovna. (2023). relationship of environmental impact assessment and environmental expertise. conference zone, 115–121. retrieved from http://conferencezone.org/index.php/cz/article/view/941
12. Alimdjanovich, R.J., Obid , K., Javlanovich, Y.D. and ugli, G.S.O. 2022. Advantages of Ultrasound Diagnosis of Pulmonary Pathology in COVID-19 Compared to Computed Tomography. Central Asian Journal of Medical and Natural Science. 3, 5 (Oct. 2022), 531-546.
13. Arifov S.S., Erkinlar Z.E., & Malikova N.N. (2021). modern methods of acne and post-acne therapy. the American journal of medical sciences and pharmaceutical research, 3(09), 147–153. https://doi.org/10.37547/TAJMSPR/Volume03Issue09-24
14. Ibragimova Malika Shavkatovna. (2022). characteristics of rehabilitation of children with cerebral palsy and speech defects. conference zone, 410–414. retrieved from http://conferencezone.org/index.php/cz/article/view/877
15. Ibragimova Malika Shavkatovna. (2022). effectiveness of hydrokinesiotherapy in the rehabilitation of children with spastic cerebral palsy. conference zone, 507–511. retrieved from http://conferencezone.org/index.php/cz/article/view/887
16. Kadirov J. F. et al. NEUROLOGICAL COMPLICATIONS OF AIDS //Journal of new century innovations. – 2022. – Т. 10. – №. 5. – С. 174-180.
17. Khakimov M.R. (2021). per una metodologia dell'insegnamento (delle lingue straniere). galaxy international interdisciplinary research journal, 9(10), 98–108. retrieved from https://giirj.com/index.php/giirj/article/view/30
18. Maxmudov S., Mavlyanova Z., Jumanov J. Analysis bioindustries indicators of body composition of individuals at a young age, not engaged in physical culture //InterConf. – 2021.
19. MS Mamasharifovich, KY Akhmadzhanovna - Art of Medicine. International Medical Scientific Journal, 2022.features of adaptation to physical loads of the cardiorespiratory system in children participated in swimming. https://artofmedicineimsj.us/index.php/artofmedicineimsj/article/view/86 https://artofmedicineimsj.us/index.php/artofmedicineimsj/article/view/86/86
20. N Ibragimova, R Tregulova, N Normatova, S Djalalov-comparative analysis of the prevalence of type 2 diabetes according to the screening and register data in Uzbekistan - Endocrine Abstracts ISSN 1470-3947 (print) | ISSN 1479-6848 (online) https://www.endocrine-abstracts.org/ea/0056/abstracts/poster-presentations-diabetes-obesity-and-metabolism/diabetes-to-include-epidemiology-pathophysiology/ea0056p342/ https://doi.org/10.1530/endoabs.56.P342
21. N.N Malikova, K.Y Karimov, K.T Boboev, S.S Arifov - The CYP17A1 rs743572 gene polymorphism and risk of development and clinical features of Acne Vulgaris in the Uzbek population.International Journal of Biomedicine, 2019. https://www.elibrary.ru/item.asp?id=38469333
22. Normatova N., Ibragimova N. Frequency of occurrence and factors of diabetic retinopathy advancement in people with DM type 2 in Uzbekistan //Endocrine Abstracts. – Bioscientifica, 2016. – Т. 41. https://www.endocrine-abstracts.org/ea/0041/ea0041ep520 https://doi.org/10.1530/endoabs.41.EP520

23. Pyagay Grigory Borisovich, & Nargiza Sayfutdinovna Ibragimova. (2023). THE effectiveness of conservative methods of treatment of actinic keratosis. conference zone, 150–155. retrieved from http://conferencezone.org/index.php/cz/article/view/948
24. Pyagay, Grigory Borisovich, & Nargiza Sayfutdinovna Ibragimova. (2023). criteria for selecting therapy for patients with actinic keratosis. conference zone, 156–161. retrieved from http://conferencezone.org/index.php/cz/article/view/949
25. Rafikovich H. M. the classification of teaching methods in higher education //journal of positive school psychology. – 2022. – с. 1582–1587-1582–1587. https://www.journalppw.com/index.php/jpsp/article/view/6098 https://www.journalppw.com/index.php/jpsp/article/view/6098/4019
26. Yakubov , J., Karimov , B., Gaybullaev , O., and Mirzakulov , M. 2022. Ultrasonic and radiological picture in the combination of chronic venous insufficiency and osteoarthritis of the knee joints. Academic Research in Educational Sciences. 5(3), pp.945–956.
27. Yakubov D. Z., Gaybullaev S. O. The diagnostic importance of radiation diagnostic methods in determining the degree of expression of gonarthrosis //UZBEK JOURNAL OF CASE REPORTS. – С. 36.
28. Yakubov Doniyor Javlanovich, Juraev Kamoliddin Danabaevich, Gaybullaev Sherzod Obid ugli, and Samiev Azamat Ulmas ugli. 2022. “INFLUENCE OF GONARTHROSIS ON THE COURSE AND EFFECTIVENESS OF TREATMENT OF VARICOSE VEINS”. Yosh Tadqiqotchi Jurnali 1 (4):347-57.
29. Z. ,Z. D. (2022). Rehabilitation and Treatment Algorithm for Patients with Ocular Ischemic Syndrome on the background of arterial hypertension. central asian journal of medical and natural sciences, 3(2), 211-213. https://doi.org/10.17605/OSF.IO/SYA5K9
30. Zaslavsky D.V., Sidikov A.A., Garyutkina L.V., Pyagai G.B., Alaeva M.D., Ibragimova N.S., Malikova N.N., Kozlova D.V. A new principle for the diagnosis morphea in the onset of the disease // Russian Journal of Skin and Venereal Diseases. - 2021. - Vol. 24. - N. 3. - P. 263-274 https://doi.org/10.17816/dv72328 https://rjsvd.com/1560-9588/article/view/72328
31. Zukhriddinovna, Z. D. (2022). Development of classification criteria for neuroretinal ischemia in arterial hypertension. central asian journal of medical and natural sciences, 3(3), 59-65. https://doi.org/10.17605/OSF.IO/K76ZT4
32. Zukhriddinovna, Z. D. (2022). clinical and metabolic peculiarities children and teenagers with arterial hypertension. central asian journal of medical and natural sciences, 3(3), 177-184. retrieved from https://cajmns.centralasianstudies.org/index.php/CAJMNS/article/view/75511
33. Zukhriddinovna, Z. D. (2022). clinical and metabolic peculiarities children and teenagers with arterial hypertension. central asian journal of medical and natural science, 3(3), 177-184. retrieved from https://cajmns.centralasianstudies.org/index.php/CAJMNS/article/view/755
34. Zukhridinovna Z. D. modern aspects of neuroprotective treatment in hypertensive retinopathy //Web of Scientist: International Scientific Research Journal. –2022. – T. 3. –No. 02. –C. 949-952. https://wos.academiascience.org/index.php/wos/article/view/947/878
35. Zukhridinovna Z. D. modern aspects of neuroprotective treatment in hypertensive retinopathy //web of scientist: international scientific research journal. – 2022. – т. 3. – №. 02. – с. 949-952. https://wos.academiascience.org/index.php/wos/article/view/949/880 https://wos.academiascience.org/index.php/wos/article/view/949

36. А.А Садиков, Н.С Ибрагимова, С.И Мавлянов - частота встречаемости кожной патологии у спортсменов при проведении углубленного медицинского осмотра (умо) и степень приверженности лечению. Безопасный спорт-2019. https://www.elibrary.ru/item.asp?id=41357327
37. А.А Садыков, Н.С Ибрагимова, А.А Юлдашев Зуд при коморбидных состояниях - va estetik tibbiyot, 2015 https://dermatology.uz/pdf/medic_juranal/Dermatologiya_N1_2015.pdf#page=29
38. Абдусаломова М А, Махмудов С М Достижения науки и образования. 2019. №11 (52). URL: https://cyberleninka.ru/article/n/optimizatsiya-mediko-sotsialnoy-reabilitatsii-pri-bolezni-dyushenna
39. Бабаев S., Бектурдиев S., Рахимов N., Джалалова D., Юсупова D., & Шаханова S. (2021). Assessment of the state of immunity in patients with tumors. in Library, 21(2), 218–225. извлечено от https://inlibrary.uz/index.php/archive/article/view/14549
40. Ваисов А. Ш., Ташкенбаева У. А., Ибрагимова Н. С. Современные аспекты этиологии, патогенеза, течения и ранней диагностики васкулитов: обзор //Новости дерматовенерол. и репрод. здоровья. – 2007. – №. 2. – С. 88.
41. Жалалова Д.З, Эшонкулов Ж.Б, Муратов З.З изменения зрительной системы у пациентов с эссенциальной артериальной гипертензией // sai. 2022. №d3. URL: https://cyberleninka.ru/article/n/izmeneniya-zritelnoy-sistemy-u-patsientov-s-essentsialnoy-arterialnoy-gipertenziey
42. И.У Салимова, Ш.Т Аюпова, Н.С Ибрагимова аспекты псориаза в дерматологии - Spirit Time, 2020 https://www.elibrary.ru/item.asp?id=42780705
43. Кадиров Ж. Ф. и др. МАГНИТНО-РЕЗОНАНСНАЯ ТОМОГРАФИЧЕСКАЯ ОЦЕНКА ПОРАЖЕНИЙ ЦЕНТРАЛЬНОЙ НЕРВНОЙ СИСТЕМЫ У БОЛЬНЫХ, ИНФИЦИРОВАННЫХ ВИРУСОМ ИММУНОДЕФИЦИТА ЧЕЛОВЕКА //Journal of new century innovations. – 2022. – Т. 10. – №. 5. – С. 157-173.
44. Мухамедов, Б., Хаджиметов, А., & Садыков, А. (2022). взаимосвязь показателей липидного состава сыворотки крови и ацетиляторного статуса у больных вирусным гепатитом с проявлениями дерматологического характера. research and education, 1(9), 231–240. retrieved from http://researchedu.org/index.php/re/article/view/976
45. Пягай, Г., Ибрагимова, Н., Мухамедов, Б., Маликова, Н., & Аллаева М. (2021). клинический случай поздней диагностики пигментной крапивницы. медицина и инновации, 1(1), 148–150. извлечено от https://inlibrary.uz/index.php/medicine_and_innovations/article/view/55
46. Тухтасинов , И. и Хакимов , М. 2021. современные взгляды на проблему дистанционного и традиционного методов обучения итальянскому языку в высших учебных заведениях . общество и инновации. 2, 2 (апр. 2021), 111–117. doi: https://doi.org/10.47689/2181-1415-vol2-iss2-pp111-117 .
47. Хакимов М. Р. development of innovative technologies in the system of higher education of the republic of uzbekistan //re-health journal. – 2020. – №. 2-2. – с. 163-164. https://www.elibrary.ru/item.asp?id=43163881
48. Хакимов М. Р. роль инновационных технологий в развитии современной системы высшего образования //editor coordinator. – 2020. – с. 189. https://uch21vek.com/assets/uch21vek_2_5_2016.pdf#page=55

49. Хакимов Мухаммадали Рафикович развитие инновационных технологий в системе высшего образования республики узбекистан // re-health journal. 2020. №2-2 (6). URL: https://cyberleninka.ru/article/n/razvitie-innovatsionnyh-tehnologiy-v-sisteme-vysshego-obrazovaniya-respubliki-uzbekistan
50. Хакимов, М. (2020). роль инновационных технологий в развитии современной системы высшего образования. interconf, (16). вилучено із https://ojs.ukrlogos.in.ua/index.php/interconf/article/view/2581
51. Хакимов, М. 2021. Дистанционное изучение иностранных языков: современные тенденции и перспективы развития. Общество и инновации. 2, 8/S (сен. 2021), 252–257. DOI: https://doi.org/10.47689/2181-1415-vol2-iss8/S-pp252-257 .
52. Хакимов, М. 2022. принципы улучшения методологии преподавания иностранного языка (на примере итальянского языка) с использованием традиционных и инновационных методов обучения в высшем учебном заведении. Общество и инновации. 3, 9/S (окт. 2022), 123–128. DOI: https://doi.org/10.47689/2181-1415-vol3-iss9/S-pp123-128 .
53. Хакимов, Мухамадали. "проблема перевода на английский язык “японского сценария” романа итальянского писателя а. барикко “шелк”." InterConf (2020).
54. Хамидов О. А., Гайбуллаев Ш. О., Хакимов М. Б. ОБЗОР МЕТОДОВ ОБРАБОТКИ ИЗОБРАЖЕНИЙ ДЛЯ ДИАГНОСТИКИ ПАТОЛОГИИ ГОЛОВНОГО МОЗГА: ПРОБЛЕМЫ И ВОЗМОЖНОСТИ //Journal of new century innovations. – 2022. – Т. 10. – №. 5. – С. 181-195.
55. Холбоев С., & Юлдашова, Н. (2022). результаты анализа основанные на миссии воз и китайской народной республики по проблеме новой коронавирусной инфекции covid-2019. Журнал кардиореспираторных исследований, 1(SI-1), 81. https://doi.org/10.26739.2181-0974-2020-SI-1-29
56. Худойкулова, Ф. В., Ибрагимова, М. Ш., Равшанова, М. З., Бурханова, Г. Л., & Абдухамидова, Д. Х. (2023). the structure, age features, and functions of hormones. pedagog, 1(5), 681-688. https://bestpublication.org/index.php/pedg/article/view/3166 https://bestpublication.org/index.php/pedg/article/view/3166/3037
57. Чуканина Д. Б., Хакимов М. Р. использование видео и аудио педагогических технологий в изучении иностранного языка //ученый xxi века. – с. 55.
58. Якубов Д. Ж., Гайбуллаев Ш. О. Влияние посттравматической хондропатии на функциональное состояние коленных суставов у спортсменов. Uzbek journal of case reports. 2022; 2 (1): 36-40. – 2022.