UDC 616-056.5-06+616.71-008.1+611.018.4+577.161.2+546.41+616.33-002.2
DOI: 10.56871/CmN-W.2024.79.24.009

VITAMIN D AND BONE METABOLISM IN DISEASES OF THE STOMACH AND DUODENUM

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For citation: Novikova VP, Seits AV. Vitamin D and bone metabolism in diseases of the stomach and duodenum. Children's Medicine of the North-West. 2024;12(3):81–96. DOI: https://doi.org/10.56871/CmN-W.2024.79.24.009

Received: 17.06.2024 **Revised: 22.07.2024** **Accepted: 10.09.2024**

Abstract. The review describes the symptoms of bone damage in diseases of the stomach and duodenum: scoliosis, poor posture, joint diseases, discrepancy between the bone age and the passport age, decreased linear growth rates and recurrent caries. The causes of bone mineral density disorders in chronic gastroduodenitis (CGD) are discussed: prolonged deficiency of micronutrients and protein due to malabsorption, significant deficiency of vitamin D and calcium. The risk factors for the development of mineral dencity in adolescents with CG and CGD, the features of bone metabolism in patients with CG that differ from those in healthy individuals, the effect of Helicobacter pylori (HP) infection on bone tissue condition and the role of vitamin D in the development of H. pylori infection are given. The review shows that currently there are insufficient data characterizing the relationship between the features of the clinical and morphological picture of chronic diseases of the upper digestive tract and Helicobacter pylori infection with the processes of osteosynthesis and remodeling of bone tissue and vitamin D. Further research is needed to develop treatment strategies for Helicobacter pylori infection, gastric neoplasia and gastric cancer.

Keywords: *bone metabolism, vitamin D, calcium, bone mineral density, chronic gastritis, Helicobacter pylori infection*

ВИТАМИН D И КОСТНЫЙ МЕТАБОЛИЗМ ПРИ ЗАБОЛЕВАНИЯХ ЖЕЛУДКА И ДВЕНАДЦАТИПЕРСТНОЙ КИШКИ

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Для цитирования: Новикова В.П., Сейц А.В. Витамин D и костный метаболизм при заболеваниях желудка и двенадцатиперстной кишки // Children's Medicine of the North-West. 2024. Т. 12. № 3. С. 81–96. DOI: https://doi.org/10.56871/CmN-W.2024.79.24.009

Поступила: 17.06.2024 **Одобрена: 22.07.2024** **Принята к печати: 10.09.2024**

Резюме. В обзоре описаны симптомы поражения костной системы при заболеваниях желудка и двенадцатиперстной кишки: сколиоз, нарушение осанки, заболевания суставов, несоответствие костного возраста паспортному, снижение показателей линейного роста тела и рецидивирующий кариес. Обсуждаются причины нарушения минеральной плотности костной ткани при хроническом гастродуодените (ХГД): продолжительный дефицит микронутриентов и белка вследствие мальабсорбции, значимый дефицит витамина D и кальция. Приводятся факторы риска развития нарушения минеральной плотности кости у подростков с ХГ и ХГД, особенности костного метаболизма у больных с ХГ, отличающиеся от показателей здоровых лиц, влияние инфицированности пилорическим хеликобактером (HP) на состояние костной ткани и описывается роль витамина D в развитии инфекции *H. pylori*. В обзоре показано, что в настоящее время данных,

которые характеризуют взаимосвязь особенностей клинико-морфологической картины хронических заболеваний верхних отделов пищеварения и хеликобактериоза с процессами остеосинтеза и ремоделирования костной ткани и витамина D, недостаточно. Необходимы дальнейшие исследования для отработки стратегий лечения хеликобактериоза, желудочных неоплазий и рака желудка.

Ключевые слова: *костный метаболизм, витамин D, кальций, минеральная плотность костей, хронический гастрит, хеликобактериоз*

In the works of the last decades it has been noted that in groups of patients of different ages suffering from gastric and duodenal diseases, bone system changes such as scoliosis, posture disorders, joint diseases [1–5], non-compliance of the bone age with the passport age, decreased linear body growth and recurrent dental caries occur with a higher frequency. Most authors report bone mineral density disorders in chronic gastroduodenitis (CGD) [5–9], considering it from the position of prolonged micronutrient and protein deficiency [10–12]. Back in 1991, A.P. Avtsyn et al. wrote: "Every physician, first of all, should be interested in factors that can damage or even destroy the mechanisms of absorption and elimination of micronutrients... The extremely common diagnosis of 'duodenitis', which occurs as often as 'gastritis', from the position of the theory of micronutrients should cause at least a careful attitude. Thus, inflammatory, dystrophic and especially atrophic changes in the duodenal mucosa are inevitably accompanied by disturbances in the absorption of trace elements" [13].

The use of dual-energy X-ray bone densitometry has shown that both children and adults with gastroduodenal diseases have reduced bone mineral density, and the degree of its reduction depends on the duration of the disease and the severity of duodenal lesions [7–10]. G.G. Haustova (2008) revealed that the level of bone mineral density (BMD) in children with CGD is interrelated with the child's age, body length and weight, morphofunctional features of the gastric and intestine mucosa: thickness of the gastric and intestine mucosa, depth of gastric glands, number of secretory granules of the main cells, number of parietal cells of the gastric mucosa, degree of vascularization of the gastric and small intestine mucosa, preservation of structural order and functional activity of the small intestine epithelium [10]. According to O.V. Guzeeva (2012), a decrease in BMD (Z-score <–2SD) in CGD in children is found in 10.6% of cases. The risk factors for the development of BMD disorders in adolescents with CGD are: the presence of an aggravated history of diseases with chronic inflammation (obesity, autoimmune and allergic diseases), the presence of comorbid somatic and allergic diseases, dental enamel disorders and superficial gastritis [5]. In adult patients, osteodensitometric study revealed a high prevalence of BMD reduction in chronic gastritis (CG). Osteopenia was found in 35% of patients in LI-LIV, in 23.3% of controls and in 52% of patients it was found in the proximal femur, while in healthy individuals osteopenia was found in 13.3%. Osteoporosis was found in 23% of patients in LI-LIV and in 13% of patients in the proximal femur, whereas no such BMD changes were found in healthy individuals [9]. Only one study did not describe differences in BMD in patients with CGD and healthy individuals [3].

Most researchers report a significant vitamin D deficiency in patients with gastroduodenal diseases, which increases with the duration of the disease [9, 10]. There is a direct correlation between serum vitamin D levels and the presence of stromal fibrosis and glandular atrophy in the gastric mucosa of adolescents with CG [5]. These results are consistent with the previously obtained data on the relationship between molecular genetic variants of VDR and the degree of inflammatory changes in the gastric mucosa of children with CG [14–16]. It can be explained by the effect of vitamin D on cell proliferation, differentiation and apoptosis [17, 18].

In adult patients with autoimmune atrophic gastritis (AAG) a significant vitamin D deficiency has also been revealed [19–21]. It correlated with the degree of atrophy of the gastric mucosa. The pathogenetic mechanism underlying this association has not been fully elucidated, but it is probably related to a decrease in vitamin D absorption against the background of gastric hypoachlorhydria [21, 22]. Several studies have reported decreased calcium absorption in patients with AAG [18, 19], while another study found no significant differences in calcium absorption in patients with autoimmune gastritis compared to

controls [20]. Since active transcellular absorption of ionized calcium in the duodenum and proximal small intestine represents the most important physiological pathway of calcium absorption and is highly dependent on vitamin D, it seems possible that vitamin D deficiency in patients with AAG explains calcium malabsorption and changes in bone mineralization [20]. In non-autoimmune CG, there is also evidence of decreased serum calcium levels [10]. There are reports of no significant difference between patients with CG and healthy controls [1, 9].

The data on BMD in AAG are controversial. A number of studies have found no significant differences in the incidence of osteoporosis between patients with AAG with vitamin D deficiency and patients with normal levels of vitamin D [20]. At the same time, it has been proven that bone mineral density is reduced in achlorhydria [22–26].

Literature data clearly indicate that not only BMD indices, but also the level of markers of bone metabolism in patients with CG differs from those of healthy individuals [1], and this level depends on the sex of patients and infection with Helicobacter pylori (HP). Thus, adolescents with chronic HP-associated gastritis were significantly more likely than their peers with HP+CG to have bone metabolism disorders in the form of lower levels of osteocalcin and higher values of blood C-terminal telopeptides (CTTP), and boys with HP-associated CG, compared to girls, were characterized by higher serum parathormone levels and lower bone mineral density against the background of a more severe course of CG [27].

It is known from a few studies that helicobacteriosis is often accompanied by a low physical development, disharmonious development, changes in bone remodeling processes and decreased bone mineral density due to impaired nutrient digestion and absorption [18, 29, 30].

It has been revealed that patients with Helicobacter-associated CG also have secondary chronic duodenitis in more than 90% of cases [31–33]. Under the influence of HP, inflammatory morphological changes develop in the duodenal mucosa, leading to a decrease in calcium absorption and its level in the body.

Previous studies have revealed some additional mechanisms of HP influence on calcium metabolism. Thus, the decrease in calcium absorption in Helicobacteriosis is associated with an increase in the absorption of competing with it nickel, the formation of which occurs in the process of destruction of bacterial urease in the stomach [3, 34]. It has been revealed that HP is able to synthesize the enzyme urease, which contains nickel in its structure. Nickel under the action of hydrochloric acid is converted to $NiCl_2$, which is easily absorbed in the stomach. In addition, the increase in the absorption of the trace element may be associated with the presence of nickel transport proteins in HP and the formation of ammonium complexes with NH_3 released during the hydrolysis of urea by bacterial urease [3, 35]. Various undesirable effects associated with toxic and mutagenic effects of this trace element may result from increased nickel intake into the organism during HP infection [11, 13]. It is probable that this effect may result in impaired bone system formation [28].

Some researchers have proposed another mechanism in CG. Thus, it is assumed that in autoimmune gastritis, antibodies to H+K+/ATPase of gastric parietal cells cross-react with a chemically similar enzyme — vacuolar H+/ATPase of osteoclasts [36–38], which is directly involved in the process of bone resorption.

Numerous studies have focused on the relationship between vitamin D deficiency and *H. pylori* infection [39–45]. The results of the published meta-analysis, which studied the relationship between serum vitamin D levels and *H. pylori*, made by M.O. Săsăran et al. in 2023, are presented in Table 1.

Despite the existence of studies that have not confirmed the relationship between helicobacteriosis and vitamin D levels [27, 51, 52, 58, 59], most previous reviews conclude that vitamin D plays an important role in the development of *H. pylori* infection. A large number of studies consider vitamin D deficiency as a risk factor for failure of *H. pylori* eradication [42, 44, 45, 63, 64]. Based on these studies, the therapeutic hypothesis of adding vitamin D_3 to classical eradication regimens emerged and the efficacy of such a regimen was proved [65].

A number of experimental works on mice confirmed the protective role of vitamin D3 in relation to gastric infection with *H. pylori* through upregulation of VDR [66, 67], enhanced activation of the antimicrobial peptide pathway VDR-cathelicidin (CAMP) [66, 67], and restoration of lysosomal degradation through activation of the protein disulfide isomerase A3 (PDIA3) receptor, which promotes calcium release from lysosomes,

ISSN 2221-2582

Table 1. Characteristics of clinical studies assessing the effect of vitamin D deficiency on *H. pylori* infection [39]

Таблица 1. Характеристика клинических исследований, в которых оценивали влияние дефицита витамина D на инфекцию *H. pylori* [39]

Автор, год / Author, year	Тип исследования / Type of study	Исследуемые группы / Study groups	Метод обнаружения *H. pylori* / Method of detection of *H. pylori*	Основной результат / Main result
Habbash et al., 2022 [45]	Ретроспективное кросс-секционное исследование / Retrospective cross-sectional study	200 взрослых пациентов / 200 adult patients: • 111 *H. pylori* положительных пациентов / 111 *H. pylori* positive patients; • 89 *H. pylori* отрицательных пациентов / 89 *H. pylori* negative patients	• Микроскопически 51% обследованных / Microscopic 51% of those examined • Дыхательный уреазный тест у 35,5% / Urease breath test in 35.5% • Оба метода у 13,5% / Both methods in 13.5%	Значительно более высокая распространенность инфекции *H. pylori* среди участников с дефицитом витамина D / Significantly higher prevalence of *H. pylori* infection among participants with vitamin D deficiency
Mut Surmeli et al., 2019 [43]	Ретроспективное кросс-секционное исследование / Retrospective cross-sectional study	254 взрослых пациента / 254 adult patients: • 43 *H. pylori* положительных пациента / 43 *H. pylori* positive patients; • 211 *H. pylori* отрицательных пациентов / 211 *H. pylori* negative patients	Гистологический метод / Histological method	Медиана уровня витамина D в сыворотке крови была значительно ниже в группе *H. pylori* положительных по сравнению с *H. pylori* отрицательных пациентов. Дефицит витамина D был значительно более частым в *H. pylori* положительной группе. Наблюдалась обратная линейная зависимость между сывороточным уровнем витамина D и положительной реакцией на *H. pylori* / The median serum vitamin D level was significantly lower in the *H. pylori* positive group compared to the *H. pylori* negative patients. Vitamin D deficiency was significantly more common in the *H. pylori* positive group. An inverse linear relationship was observed between serum vitamin D level and *H. pylori* positivity
Assaad et al., 2018 [46]	Кросс-секционное исследование / Cross-sectional study	294 взрослых пациента / 294 adult patients: • 154 *H. pylori* положительных пациента / 154 *H. pylori* positive patients; • 140 *H. pylori* отрицательных пациентов / 140 *H. pylori* negative patients	Гистологическое исследование биопсийных образцов желудка / Histological examination of gastric biopsy samples	Значимо более высокая распространенность уровня витамина D в сыворотке крови <20 нг/мл среди исследуемой группы *H. pylori* / Significantly higher prevalence of serum vitamin D levels <20 ng/mL among the *H. pylori* study group
Bashir et al., 2016 [47]	Интервенционное моноцентровое открытое пилотное исследование / Interventional monocentric open-label pilot study	15 здоровых взрослых / 15 healthy adults: • 3 пациента с диагнозом *H. pylori* / 3 patients diagnosed with *H. pylori*	Гистологическое исследование биопсийных образцов желудка / Histological examination of gastric biopsy samples	В подгруппе, у которой была диагностирована инфекция *H. pylori*, 8-недельный режим приема добавок с высоким пероральным содержанием витамина D_3 приводил к значительному снижению колонизации слизистой оболочки желудка *H. pylori* / In the subgroup diagnosed with *H. pylori* infection, an 8-week high-dose oral vitamin D_3 supplementation regimen resulted in a significant reduction in gastric mucosal colonization with *H. pylori*

Автор, год / Author, year	Тип исследования / Type of study	Исследуемые группы / Study groups	Метод обнаружения *H. pylori* / Method of detection of *H. pylori*	Основной результат / Main result
Shafrir et al., 2021 [44]	Ретроспективное кросс-секционное исследование / Retrospective cross-sectional study	150 483 взрослых пациента / 150,483 adult patients: • 75 640 *H. pylori* положительных пациентов / 75,640 *H. pylori* positive patients; • 74 843 *H. pylori* отрицательных пациента / 74,843 H. pylori negative patients	Дыхательный уреазный тест в 99% случаев / Urea breath test in 99% of cases Анализ кала на антиген в остальных случаях / Stool antigen test in the rest	Средние уровни витамина D в сыворотке крови были значительно выше в отрицательной группе *H. pylori*. Наблюдалась обратная линейная зависимость между сывороточным уровнем витамина D и положительной реакцией на *H. pylori*. Более высокая распространенность *H. pylori* среди лиц со значениями витамина D <20 нг/мл / Mean serum vitamin D levels were significantly higher in the *H. pylori* negative group An inverse linear relationship was observed between serum vitamin D levels and *H. pylori* positivity Higher prevalence of *H. pylori* among individuals with vitamin D values < 20 ng/mL
Han et al., 2019, [48]	Многоцентровое обсервационное и проспективное когортное исследование / A multi-center observational and prospective cohort study	672 взрослых пациента / 672 adult patients: • 415 *H. pylori* положительных пациента / 415 *H. pylori* positive patients; • 257 *H. pylori* отрицательных пациентов / 257 *H. pylori* negative patients	Дыхательный тест на мочевину / Urea breath test	Значительно более низкие уровни витамина D в сыворотке крови в группе *H. pylori* / Significantly lower serum vitamin D levels in the *H. pylori* group
Assaad et al., 2019 [49]	Ретроспективное кросс-секционное исследование / Retrospective cross-sectional study	460 взрослых пациентов / 460 adult patients: • 225 *H. pylori* положительных пациентов / 225 H. pylori positive patients; • 235 *H. pylori* отрицательных пациентов / 235 *H. pylori* negative patients	Гистологическое исследование биопсийных образцов желудка / Histological examination of gastric biopsy samples	Значимо более высокая распространенность недостаточности витамина D среди исследовательской группы *H. pylori*. Обнаружена обратная зависимость между двумя однонуклеотидными полиморфизмами TLR4 и уровнями витамина D / Significantly higher prevalence of vitamin D deficiency among the study group *H. pylori*. Inverse association found between two TLR4 single nucleotide polymorphisms and vitamin D levels
Mohammed et al., 2021 [50]	Ретроспективное кросс-секционное исследование / Retrospective cross-sectional study	100 здоровых женщин с ожирением / 100 healthy obese women: • пациенты 1–3 группы с недостаточностью витамина D + группа 2–10 пациентов с недостаточностью витамина D / group 1–3 vitamin D deficient patients + group 2–10 vitamin D-deficient patients H. pylori; • *H. pylori* отрицательная — группа 3–13 пациентов с дефицитом витамина D / Group 3–13 vitamin D-deficient patients *H. pylori*+;	Обнаружение специфических сывороточных антител (IgM и IgG), направленных против *H. pylori* / Detection of specific serum antibodies (IgM and IgG) directed against *H. pylori*	Различия в показателях положительного результата на антитела к *H. pylori* в сыворотке крови наблюдались только между группами 3 и 4, в которых наблюдался дефицит витамина D / Differences in serum *H. pylori* antibody positivity were observed only between Groups 3 and 4, which had vitamin D deficiency

ISSN 2221-2582

ISSN 2221-2582

Continuation of the table 1 / Продолжение табл. 1

Автор, год / Author, year	Тип исследования / Type of study	Исследуемые группы / Study groups	Метод обнаружения *H. pylori* / Method of detection of *H. pylori*	Основной результат / Main result
		• *H. pylori* положительная — группа 4–74 пациентов с дефицитом витамина D *H. pylori*– /group 4–74 vitamin D-deficient patients *H. pylori*–		
Chen et al., 2016 [51]	Проспективное исследование на базе сообщества / A community-based prospective study	2113 взрослых пациентов / 2113 adult patients: • 557 пациентов с метаболическим синдромом / 557 patients with metabolic syndrome; • 1556 пациентов без метаболического синдрома / 1556 patients without metabolic syndrome	Дыхательный уреазный тест / Urea breath test	Уровни витамина D были одинаковыми среди включенной популяции, независимо от инфекционного статуса *H. pylori*. Субъекты, инфицированные *H. pylori* и с дефицитом витамина D, были наиболее восприимчивы к развитию метаболического синдрома / Vitamin D levels were similar among the included population, regardless of infection status *H. pylori*. Subjects infected with *H. pylori* and with vitamin D deficiency were most susceptible to developing metabolic syndrome
Gerig et al., 2013 [52]	Ретроспективное кросс-секционное исследование / Retrospective cross-sectional study	404 взрослых пациента с ожирением, перенесших бариатрическую операцию / 404 obese adult patients undergoing bariatric surgery: • 85 *H. pylori* положительных пациентов / 85 *H. pylori* positive patients; • 319 *H. pylori* отрицательных пациентов / 319 *H. pylori* negative patients	Гистопатологическое исследование биопсийных образцов желудка / Histological examination of gastric biopsy samples	Не было существенных различий в уровнях витамина D между двумя исследуемыми группами / There were no significant differences in vitamin D levels between the two study groups
Mihalache et al., 2016 [53]	Перекрестное обсервационное исследование / Cross-sectional, observational study	93 взрослых пациента с ожирением / 93 obese adults: • 47 пациентов с положительным результатом на *H. pylori* / 47 patients positive for *H. pylori*; • 46 пациентов с отрицательным результатом на *H. pylori* / 46 patients negative for *H. pylori*	Гистопатологическое исследование биопсийных образцов желудка / Histological examination of gastric biopsy samples	Несколько более высокие средние уровни витамина D в сыворотке крови были обнаружены у пациентов, инфицированных инфекцией *H. pylori*, но эта разница не достигла статистической значимости / Slightly higher mean serum vitamin D levels were found in patients infected with *H. pylori*, but this difference did not reach statistical significance
Mirza et al., 2022 [54]	Проспективное исследование «случай–контроль» / Prospective case–control study	800 взрослых субъектов / 800 adult subjects: • 400 пациентов с лихорадкой денге (*H. pylori* положительный и *H. pylori* отрицательный) / 400 dengue patients (*H. pylori* positive and *H. pylori* negative)	Дыхательный уреазный тест / Urea breath test	У пациентов с лихорадкой денге и коинфекцией, вызванной *H. pylori*, уровни витамина D были значительно ниже, чем у здоровой контрольной группы, у которой была диагностирована инфекция *H. pylori*. Пациенты с лихорадкой денге, коинфицированные *H. pylori*, имели более высокую вероятность дефицита витамина D, чем те, у кого бактериальная инфекция не была обнаружена /

Автор, год / Author, year	Тип исследования / Type of study	Исследуемые группы / Study groups	Метод обнаружения *H. pylori* / Method of detection of *H. pylori*	Основной результат / Main result
		• 400 здоровых людей из контрольной группы (*H. pylori* положительный и *H. pylori* отрицательный) / 400 healthy controls (*H. pylori* positive and *H. pylori* negative)		Patients with dengue and *H. pylori* coinfection had significantly lower vitamin D levels than healthy controls diagnosed with *H. pylori* infection Dengue patients coinfected with *H. pylori* were more likely to be vitamin D deficient than those without bacterial infection
Nasri et al., 2007 [55]	Кросс-секционное исследование / Cross-sectional study	36 взрослых пациентов с терминальной стадией почечной недостаточности, находящихся на гемодиализе / 36 adult patients with end-stage renal disease undergoing hemodialysis	Обнаружение специфических сывороточных антител (IgG), направленных против *H. pylori* / Detection of specific serum antibodies (IgG) directed against *H. pylori*	Значимая положительная связь между уровнем витамина D в сыворотке крови и титром специфических антител IgG к *H. pylori* / Significant positive association between serum vitamin D level and titer of specific IgG antibodies to *H. pylori*
Bener et al., 2020 [56]	Проспективное исследование «случай–контроль» / Prospective case–control study	1058 взрослых субъектов / 1058 adult subjects: • 529 пациентов с сахарным диабетом 2-го типа / 529 patients with type 2 diabetes; • 529 здоровых людей соответствующего возраста / 529 healthy age-matched controls	Обнаружение специфических сывороточных антител (IgA и IgG), направленных против *H. pylori* / Detection of specific serum antibodies (IgA and IgG) directed against *H. pylori*	Значительно более низкие уровни витамина D в сыворотке крови у пациентов с сахарным диабетом 2-го типа и серопозитивностью IgA/IgG по сравнению с контрольной группой с положительными сывороточными антителами / Significantly lower serum vitamin D levels in patients with type 2 diabetes and IgA/IgG seropositivity compared to controls with positive serum antibodies
Zawada et al., 2023 [57]	Кросс-секционное исследование / Cross-sectional study	103 взрослых пациента с сахарным диабетом 1-го типа / 103 adult patients with type 1 diabetes mellitus: • 31 *H. pylori* положительный пациент / 31 *H. pylori* positive patients; • 72 *H. pylori* отрицательных пациента / 72 *H. pylori* negative patients	Анализ кала на антиген *H. pylori* / Stool testing for *H. pylori* antigen	Значительно более низкие уровни витамина D в сыворотке крови у пациентов с инфекцией *H. pylori*. Значимая связь между более низкими уровнями витамина D в сыворотке крови и положительными тестами на антиген *H. pylori* в стуле / Significantly lower serum vitamin D levels in patients with *H. pylori* infection. Significant association between lower serum vitamin D levels and positive stool tests for *H. pylori* antigen
Agin et al., 2021 [58]	Проспективное исследование «случай–контроль» / Prospective case–control study	291 ребенок, которым была выполнена эндоскопия верхних отделов пищеварительной системы: 38 пациентов с язвенной болезнью желудка и 253 пациента с болезнью двенадцатиперстной кишки / 291 children who underwent upper gastrointestinal endoscopy: 38 patients with gastric ulcer and 253 patients with duodenal ulcer	Гистологическое исследование биопсийных образцов желудка / Histological examination of gastric biopsy samples	Значимая связь между более низкими уровнями витамина D в сыворотке крови и наличием язвенной болезни. Отсутствие изменений в уровнях витамина D в связи с инфекцией *H. pylori* / Significant association between lower serum vitamin D levels and the presence of peptic ulcer. No change in vitamin D levels associated with *H. pylori* infection

ISSN 2221-2582

ISSN 2221-2582

Ending of the table 1 / Окончание табл. 1

Автор, год / Author, year	Тип исследования / Type of study	Исследуемые группы / Study groups	Метод обнаружения *H. pylori* / Method of detection of *H. pylori*	Основной результат / Main result
Urganci et al., 2020 [59]	Проспективное кросс-секционное исследование / Prospective cross-sectional study	100 детей с хроническим гастритом / 100 children with chronic gastritis: • 72 *H. pylori* положительных пациента / 72 *H. pylori* positive patients • 28 *H. pylori* отрицательных пациентов / 28 *H. pylori* negative patients	По крайней мере два из трех обследований / At least two of three examinations: гистологическое исследование образцов биопсии желудка / histological examination of gastric biopsy samples; бактериологическое исследование образцов биопсии желудка / bacteriological examination of gastric biopsy samples; уреазный экспресс-тест с биоптатом слизистой оболочки желудка / rapid urease test with gastric mucosa biopsy serum	Уровни витамина D в сыворотке крови были одинаковыми между двумя исследуемыми группами / Vitamin D levels were similar between the two study groups
Gao et al., 2020 [60]	Ретроспективное кросс-секционное исследование / Retrospective cross-sectional study	6896 внешне здоровых младенцев и детей ясельного возраста / 6896 apparently healthy infants and toddlers: • 2113 Серопозитивные лица по *H. pylori* / 2113 *H. pylori* seropositive individuals • 4783 Серонегативные лица по *H. pylori* / 4783 *H. pylori* seronegative individuals	Обнаружение специфических сывороточных антител (IgG), направленных против *H. pylori* / Detection of specific serum antibodies (IgG) directed against *H. pylori*	Значительно более высокая распространенность дефицита витамина D среди серопозитивных детей, инфицированных *H. pylori* / Significantly higher prevalence of vitamin D deficiency among *H. pylori* seropositive children

lysosomal acidification and, consequently, elimination of *H. pylori* through the autolysosomal pathway [68]. Synthetic production of vitamin D-derived indene compounds has been shown to result in selective antibacterial effect against *H. pylori* [69, 70]. In particular, vitamin D products, such as vitamin D3 product 1 (VDP1), delay effects against *H. pylori* by inducing collapse of the cell membrane structure of bacteria [71]. The inhibitory effect of 1α,25-dihydroxyvitamin D_3 on *H. pylori*-induced apoptosis of gastric epithelial cells was proved [72].

Gastric mucosal cells from patients infected with *H. pylori* showed a significant increase in VDR expression compared to the healthy control group [73]. A significant correlation was also found between FokI and ApaI polymorphisms of the *VDR* gene and BsmI genotypes of the *VDR* gene and *H. pylori* infection [74]. The other three polymorphisms studied, namely FokI, ApaI and TaqI, showed no significant variations in genotype distribution between the two groups studied [75].

Several studies have shown significantly lower levels of 25-OHvitD in patients with gastric neuroendocrine neoplasms (NEN) compared to patients without gastric NEN. The pathogenetic mechanism leading to this association has been attributed to the pleiotropic effects of vitamin D [47, 51, 76, 77]. In the last few years, a number of studies have also focused on the antitumor properties of vitamin D in various solid neoplasms [48, 51, 74]. Tumor suppressor protein 3 (VDUP1) was found to increase the regulation of vitamin D_1 (VDUP67), which has been shown to be protective against gastric carcinogenesis [3].

Nevertheless, there is currently insufficient data that characterize the relationship between the clinical and morphological features of chronic upper digestive diseases and helicobacteriosis and the processes of osteosynthesis and bone remodeling and vitamin D. Further studies are needed in order to refine strategies for the treatment of helicobacteriosis, gastric neoplasia and gastric cancer.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

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