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Selenium plasma levels in children with Helicobacter pylori-associated diseases of the upper gastrointestinal tract

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Despite the success of the treatment of infected individuals, *Helicobacter pylori* infection remains the most common human bacterial pathogen, infecting half of the world's population. In a large part of people, *H. pylori* causes gastroduodenal diseases, in particular, chronic antral gastritis and ulcer disease. The possible role of selenium in the course of chronic inflammatory *H. pylori*-associated pathology of the upper gastrointestinal tract in children has not yet been fully investigated and understood.

The aim is to determine selenium plasma levels in children with *Helicobacter pylori*-associated diseases of the upper gastrointestinal tract.

Materials and methods. The study included 135 school-age children with *Helicobacter pylori*-associated diseases of the upper gastrointestinal tract, who made up the main study group (55 children with chronic gastritis (CG), 57 children with chronic gastroduodenitis (CGD), 23 children with duodenal ulcer (DU), and 20 practically healthy age-matched children were the comparison group. Quantitative measurements of plasma selenium were performed using inductively coupled plasma mass spectrometry (MS-ICP) on an Optima 2000 DV spectrometer (Perkin Elmer, USA).

Results. The lowest level of plasma selenium was registered in children with *H. pylori*-negative DU (67.81 ± 2.67 μg/l), while in children with *H. pylori*-associated DU, its level was higher – 73.56 ± 2.34 μg/l ($p < 0.05$), however, it did not reach the level in children of the comparison group. A similar direction of changes in the selenium plasma concentration was observed in children with CGD: higher levels of selenium were detected in children with *H. pylori*-positive CGD compared to *H. pylori*-negative CGD (75.61 ± 2.48 μg/l and 70.99 ± 2.31 μg/l, respectively, $p < 0.05$).

Conclusions. Significantly lower levels of plasma selenium in children with chronic destructive-inflammatory diseases of the upper gastrointestinal tract were found, which could be explained by the acute phase of inflammation in the mucous membrane of the stomach and duodenum resulting in a decrease in selenium absorption. In *H. pylori*-positive children, the level of selenium was significantly higher compared to *H. pylori*-negative children indicating a possible role of selenium in the pathogenesis and further progression of *H. pylori*-associated diseases.

Ключові слова: діти, *H. pylori*-асоційовані захворювання, селен.

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Рівень селену в плазмі крові дітей із Helicobacter pylori-асоційованими захворюваннями верхніх відділів шлунково-кишкового тракту

Т. В. Сорокман, І. С. Сокольник

Незважаючи на успіхи в лікуванні хворих, *Helicobacter pylori* інфекція залишається найпоширенішим бактеріальним патогеном людини, інфікуючи половину населення світу. У значної частки людей *H. pylori* спричиняє гастродуоденальні захворювання, зокрема хронічний антральний гастрит і виразкову хворобу. Можлива роль селену в перебігу хронічної запальної *H. pylori*-асоційованої патології верхніх відділів шлунково-кишкового тракту в дітей досі не повністю досліджена та зрозуміла.

Мета роботи – визначити рівень селену в плазмі крові дітей із *Helicobacter pylori*-асоційованими захворюваннями верхніх відділів шлунково-кишкового тракту.

Матеріали та методи. У дослідження залучили 135 дітей шкільного віку, хворих *Helicobacter pylori*-асоційовані захворювання верхніх відділів шлунково-кишкового тракту, які сформували основну групу дослідження (55 дітей із хронічним гастритом (ХГ), 57 осіб із хронічним гастродуоденітом (ХГД), 23 пацієнти з виразкою дванадцятипалої кишки (ВДПК). Обстежили також 20 практично здорових дітей відповідного віку, котрих залучили у групу порівняння. Кількісно селен у плазмі крові визначали за допомогою мас-спектрометрії з індуктивно зв'язаною плазмою (МС-ІСП) на спектрометрі Optima 2000 DV (Perkin Elmer, США).

Результати. Найнижчий рівень селену в плазмі крові зареєстрували в дітей, хворих на *H. pylori*-негативну ВДПК (67,81 ± 2,67 мкг/л), а в дітей із *H. pylori*-асоційованою ВДПК його рівень вищий, становить 73,56 ± 2,34 мкг/л ($p < 0,05$), але не досяг рівня в дітей групи порівняння. Аналогічний напрям змін концентрації селену в плазмі крові спостерігали в дітей із ХГД: вищі показники селену зафіксовано в дітей із *H. pylori*-позитивним ХГД порівняно з *H. pylori*-негативним ХГД (75,61 ± 2,48 мкг/л і 70,99 ± 2,31 мкг/л відповідно, $p < 0,05$).

Висновки. Визначили вірогідно нижчі рівні селену в плазмі крові дітей, хворих на хронічні деструктивно-запальні захворювання верхніх відділів шлунково-кишкового тракту. Це можна пояснити гострою фазою запалення слизової оболонки шлунка та дванадцятипалої кишки, що призводить до зниження всмоктування селену. У *H. pylori*-позитивних дітей рівень селену вірогідно вищий порівняно з *H. pylori*-негативними дітьми; це вказує на можливу роль селену в патогенезі та наступному прогресуванні *H. pylori*-асоційованих захворювань.

Helicobacter pylori (*H. pylori*) has been recognized as a major human pathogen for almost four decades [1]. Despite successful treatment of infected individuals, this infection remains the most common human bacterial pathogen, infecting half of the world's population [2,3]. In a large part of people, *H. pylori* causes gastroduodenal diseases, in particular, chronic antral gastritis and ulcer disease [4–9]. A literature search has revealed more than 45,000 publications on issues of this bacterium [10–14]. Much has been learned about the infection epidemiology, biology, genetics, pathophysiology, disease manifestation, diagnosis, and treatment [15–17]. However, problems regarding modes of infection transmission remain serious and unresolved despite numerous epidemiological studies, as well as determinants of the disease manifestation continue to be insufficiently examined, including many aspects of the host-pathogen interaction [18].

H. pylori infection affects gastric secretion and absorption of nutrients. Micronutrient deficiencies caused by this infection can lead to disruption of biological and immunological activity [19]. A persistent gastric mucosal inflammatory response to *H. pylori* infection can alter gastric physiology and, as a result, *H. pylori* can compromise the nutritional status of infected patients, interfere with the absorption of various nutrients, and cause a variety of clinical symptoms [20].

Deficiency of microelements, in particular selenium, can result in harmful consequences due to clinical effects, such as a decrease in immunological protection, cognitive impairment, anemia, growth retardation, and oxidative stress [21–24]. Over the past few decades, there has been a growing interest of researchers in selenium as one of the key microelements in ensuring the functioning of the enzymatic antioxidant system of the human body [25–27]. The possible role of selenium in the course of chronic inflammatory *H. pylori*-associated pathology of the upper gastrointestinal tract in children has not yet been fully examined and understood.

Aim

The aim is to determine selenium plasma levels in children with *Helicobacter pylori*-associated diseases of the upper gastrointestinal tract.

Materials and methods

The study included 135 school-age children with *Helicobacter pylori*-associated diseases of the upper gastrointestinal tract, who were the main study group (55 children with chronic gastritis (CG), 57 children with chronic gastroduodenitis (CGD), 23 children with duodenal ulcer (DU), and 20 age-matched practically healthy children were the comparison group. Verification of the diagnosis was carried out in line with the protocol according to the order of the Ministry of Health of Ukraine No. 59 [28] based on the data of fibrogastroduodenoscopy using a video endoscopy system OLYMPUS EVIS EXERA II CV-165 and a video gastroscope GIF-Q165 as well as the Houston modification of the Sydney classification of chronic gastritis (1996) with assessments of *H. pylori* infection topography and morphology by using the rapid urease test and determining specific immunoglobulins of classes M, A and G to *H. pylori* CagA protein in blood serum according to the generally accepted method.

Quantitative determination of plasma selenium was performed using inductively coupled plasma mass spectrometry (MS-ICP) with a spectrometer Optima 2000 DV (Perkin Elmer, USA). Blood sampling was carried out in a procedure room from the cubital vein in the morning on an empty stomach in a volume of at least 5 ml in a standard glass tube without the use of a coagulation activator. After centrifugation, the plasma was transferred to test tubes and stored at a temperature of -70 ºC until analysis. The concentration of chemical elements was estimated in μg/l.

The study was conducted on the basis of the Gastroenterology Department of the Chernivtsi Regional Clinical Hospital during 2020–2022, following the main provisions of the GCR (1996), the Helsinki Declaration of the World Medical Association on the ethical principles of conducting scientific medical research, and after signing informed consent by parents and patients. Ethics committee approval was received for this study.

Statistical Package software, version 10 (USA), was used for data analysis. Student's t test and Wilcoxon rank sum test were used to assess statistical differences between means and to compare continuous variables. Statistical significance was defined as a value of $p < 0.05$.

Results

The distribution of children by age, sex, nosology depending on the *H. pylori* presence is presented in *Table 1*.

The mean level of plasma selenium in children with inflammatory and destructive diseases of the upper gastrointestinal tract was 73.12 ± 9.45 μg/l, in children of the comparison group – 85.42 ± 9.44 μg/l ($p > 0.05$). We have not found sex and age differences in plasma selenium levels. The lowest level of plasma selenium was registered in children with *H. pylori*-negative DU (67.81 ± 2.67 μg/l), while in children with *H. pylori*-associated DU, its level was higher, 73.56 ± 2.34 μg/l ($p < 0.05$), however, it did not reach the level in children of the comparison group (*Fig. 1*).

A similar direction of changes in the plasma selenium concentration was observed in children with CGD (*Fig. 2*): higher levels of selenium were recorded in children with *H. pylori*-positive CGD compared to those in *H. pylori*-negative CGD (75.61 ± 2.48 μg/l and 70.99 ± 2.31 μg/l, respectively, $p < 0.05$).

It is worth noting that the plasma selenium concentration in children with chronic inflammatory-destructive pathology of the upper gastrointestinal tract depended on the functional state of the stomach, in particular, the acid-producing function. Thus, in children with preserved acid-producing function of the stomach, the concentration of selenium was close to the level in children of the comparison group, while the level of selenium was lower with an increase in the stomach acid secretion (*Fig. 3*).

Discussion

H. pylori remains a major public health problem worldwide [29]. Currently, the selenium involvement in the regulation of cellular enzymatic processes, metabolism of nucleic acids, proteins, hormones and vitamins is being

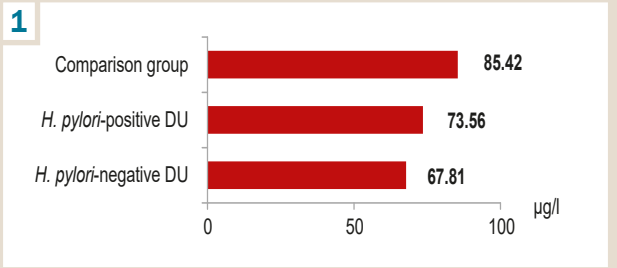
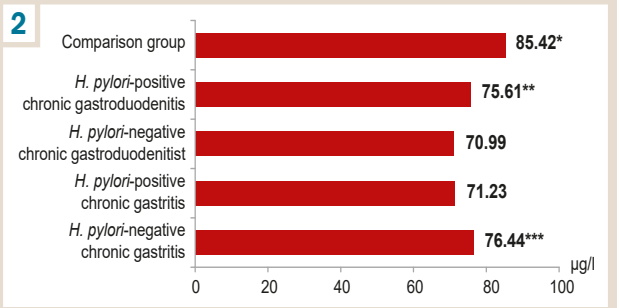


Fig. 1. Levels of plasma selenium in children with DU depending on the presence of *H. pylori*.

Fig. 2. Plasma selenium concentration in children with chronic gastritis and chronic gastroduodenitis depending on the presence of *H. pylori* infection. ***:** significant difference between indicators in children of the comparison group and the main group; ****:** significant difference between indicators in children with *H. pylori*-positive chronic gastroduodenitis and *H. pylori*-negative gastroduodenitis; *****:** significant difference between indicators in children with *H. pylori*-positive chronic gastritis and *H. pylori*-negative gastritis ($p < 0.05$).

Fig. 3. Plasma selenium concentration in children depending on the state of the gastric acid secretion. ***:** the difference is significant, $p < 0.05$.



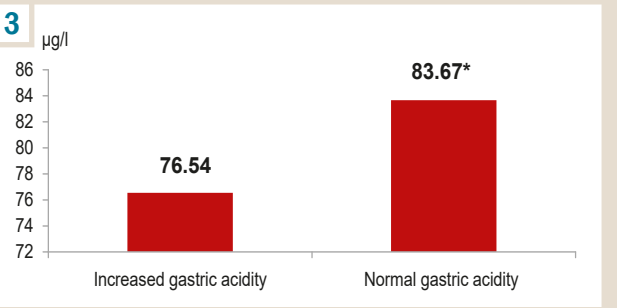


Table 1. Distribution of children by age, sex, nosology

Indicator	*H. pylori* (+), n = 68	*H. pylori* (-), n = 67
Mean age (years)	13.4 ± 1.3	14.1 ± 1.4
Sex		
Boys	36	30
Girls	32	38
CG (n = 55)	28	27
CGD (n = 57)	21	36
DU (n = 23)	19	4

CG: chronic gastritis; **CGD:** chronic gastroduodenitis; **DU:** duodenal ulcer.

discussed [30]. It has been demonstrated that selenium is a component of more than 300 enzymes, has a direct physiological effect on cell membranes, changing their permeability or activity of membrane enzymes [31]. Absorption of selenium occurs in the upper part of the small intestine, and mainly in the duodenum, where 40–45 % of the microelement is absorbed. With normal nutrition, primary selenium deficiency is quite rare, since a mixed diet completely covers the need for this element [32]. The antiulcerogenic effect of selenium is noted based on its ability to stabilize lysosome membranes, inhibit free radical oxidation and lipid peroxidation [33–35].

Our study has revealed the decrease in the plasma selenium content in children with chronic destructive-inflammatory pathology of the upper gastrointestinal tract. Similar results were obtained when conducting research among adults with various forms of chronic gastritis. This can be explained by the acute phase of inflammation of the gastric and duodenum mucous membrane, which leads to a decrease in the absorption of selenium. In children with *H. pylori* infection, higher levels of plasma selenium have been detected. By affecting gastric secretions and acidity, *H. pylori* infection affects the digestion and assimilation of nutrients, including essential trace elements, particularly selenium.

Selenium is an important component of antioxidant protection. Selenium deficiency can cause various complications, such as disorders of the immune response, oxidative stress, malignant tumors and increased susceptibility to infections [36].

Some studies have reported an inverse relationship between the risk of death from gastric cardia cancer and basal serum selenium concentrations [37]. As a component of selenoproteins (mainly selenoproteins S and K), selenium can downregulate inflammatory signaling pathways involved in the pathogenesis of destructive inflammatory diseases, including the production of inflammatory cytokines [38,39]. Deficiency or excess of microelements caused by *H. pylori* infection can be accompanied by various clinical symptoms.

Despite the research on this topic, the possible role of microelements in *H. pylori* infection is still not fully understood. In our region, there were no studies on the effect of *H. pylori* infection on the level of plasma selenium. This is the first such study among children that we know of. There are insufficient data on plasma selenium levels in patients with *H. pylori*-associated CG, CGD, and DU. It is believed that such studies are necessary to determine possible *H. pylori* mechanisms of exposure.

Conclusions

1. Significantly lower levels of plasma selenium in children with chronic destructive-inflammatory diseases of the upper gastrointestinal tract have been found, which can be explained by the acute phase of inflammation of the mucous membrane of the stomach and duodenum leading to a decrease in selenium absorption.

2. In *H. pylori*-positive children, the level of selenium was significantly higher compared to that in *H. pylori*-negative children indicating the possible role of selenium in the pathogenesis and further progression of *H. pylori*-associated diseases.

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