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Serum levels of neurokinin B in patients with non-alcoholic fatty liver disease and intestinal lesions after COVID-19

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Abstract. ***Background.*** *The study of neuropeptides, including substance P, neurokinins, may reveal possible mechanisms of the progression of gastrointestinal lesions with the formation of motility disorders in patients with coronavirus disease 2019 (COVID-19), especially in metabolically associated diseases such as non-alcoholic fatty liver disease (NAFLD), obesity,* type 2 diabetes mellitus. Aim of the research: *to determine the peculiarities of changes in serum neurokinin B (NK-B) levels in patients with NAFLD after COVID-19.* ***Materials and methods.*** *The study included 104 patients with NAFLD and intestinal lesions at the outpatient stage of follow-up after COVID-19 (they formed the main group of those being treated (group I)). Group II (comparison one) included 78 patients with NAFLD who did not have neither COVID-19, nor complaints indicating intestinal lesions. All examined patients were tested for NK-B levels in blood serum.* ***Results.*** *Complaints indicating intestinal lesions in patients with NAFLD after COVID-19 were more often manifested by changes in the act of defecation, namely constipation was diagnosed in 51.0 % of cases ($p < 0.001$), a tendency to diarrhea — in 26.9 %, and in 22.1 % of patients in group I, constipation followed by diarrhea was diagnosed. Among NAFLD patients, a significant increase in serum NK-B levels with minimal deviations from the norm was found in group II (1.1-fold; $p < 0.05$), while in group I, significant deviations from the norm were diagnosed (3.0-fold; $p < 0.001$). The lowest levels of NK-B were detected in intestinal damage manifested by constipation. In patients with diarrhea in NAFLD after COVID-19, the level of NK-B was maximal and 6.2 times ($p < 0.001$) higher than that of the control group.* **Conclusions.** *Among patients with NAFLD, intestinal damage after COVID-19 is more often manifested by constipation (in 51.0 % of cases). In patients with NAFLD after COVID-19, changes in the level of neurokinin B in the blood serum were found, with its minimum in constipation ((0.173 ± 0.009) pg/ml; $p < 0.01$), and maximum values in patients with diarrhea (an increase to (1.782 ± 0.023) pg/ml; $p < 0.001$).*

Keywords: *non-alcoholic fatty liver disease; intestinal lesions; COVID-19; neurokinin B*

Introduction

The 2019 coronavirus disease (COVID-19), caused by a new RNA-beta enveloped coronavirus, called the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a significant public health problem for all countries of the world. Although COVID-19 is primarily characterized by respiratory symptoms, it has become apparent that it can also cause a number of extrapulmonary manifestations. It is known that people with chronic diseases have a more severe course of COVID-19, in particular those with obesity, diabetes, and metabolic syndrome. Liver steatosis, which is often diagnosed in patients with obesity and diabetes mellitus, has been recognized as an independent predictor of COVID-19 severity [1–3].

In 2016, a meta-analysis of studies published between 1990 and 2015 provided evidence that the global prevalence of nonalcoholic fatty liver disease (NAFLD) was about 25.0 %, making it the most common cause of chronic liver disease (CLD). The subsequent data from the Global Burden of Disease study have supplemented this data and provided evidence that NAFLD is the fastest-growing global contributor to the disease burden related to the complications of CLD, including cirrhosis and liver cancer. Furthermore, the most recent data from the United States' United Network of Organ Sharing (UNOS) indicates that currently NAFLD is the second indication for all liver transplants and is rapidly becoming the top indication for liver transplantation among

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those listed for hepatocellular carcinoma. This rapid increase is driven by the pandemic of obesity and type 2 diabetes mellitus (T2DM). In this context, the number of metabolic conditions that one carries not only increases the risk of having NAFLD but also the risk of progression to advanced liver disease and mortality. In addition to adverse clinical outcomes such as increased mortality, NAFLD is also associated with a significant economic burden and impairment of patients' health-related quality of life [4]. At the same time, NAFLD is an independent predictor that increases the impact of obesity on the prognosis of COVID-19 [5].

SARS-CoV-2 is known to infect cells primarily by binding to the ACE 2 (angiotensin I converting enzyme 2) receptor. A significant level of ACE 2 expression is observed in lung tissue, which determines its vulnerability to infection, but this receptor is also expressed in the heart, liver, and intestine. Possible mechanisms of SARS-CoV-2 virus infection of the gastrointestinal tract include the following: 1) dysregulation of ACE 2, whose deficiency increases the susceptibility of the intestine to inflammation. It is possible that SARS-CoV-2, which reduces ACE 2 expression in the lungs, similarly reduces it in the gut; 2) changes in the composition and function of the microflora as a result of hypoxia caused by COVID-19; 3) disruption of the intestinal barrier due to local inflammation or virus replication; 4) involvement of the gut-brain axis. The intestinal nervous system can be damaged either directly by the viral infection or by components of the immune response, resulting in increased diarrhea and possibly stimulation of the vagus nerve, which causes vomiting [6].

Therefore, the study of neuropeptides, including substance P, neurokinins, may reveal possible mechanisms of the progression of gastrointestinal lesions with the formation of motor dysfunction in patients with COVID-19, especially in metabolically associated diseases such as NAFLD, obesity, type 2 diabetes mellitus.

Objective. To determine the peculiarities of changes in serum neurokinin B levels in patients with NAFLD after COVID-19.

Materials and methods

The examination and treatment of patients was carried out at the clinical base of the Department of Propedeutics of Internal Diseases of the School of Medicine of the State Higher Educational Establishment "Uzhhorod National University". The study included 104 patients with NAFLD and intestinal lesions who were treated in the gastroenterological and endocrinological departments of the Novak ZOCL of the Health Care Facilities of the Health Care District, as well as at the family doctor's place of residence during the outpatient stage of follow-up after COVID-19 (they formed the main group of those being treated (group I)). From the anamnesis data, it was found that all the examined patients had a confirmed diagnosis of SARS-CoV-2 virus infection (positive polymerase chain reaction to SARS-CoV-2 RNA — SARS-CoV-2 RdRP gene, SARS-CoV-2 E gene), mostly of mild or moderate severity. Group II (comparison group) included 78 patients with NAFLD who did not have COVID-19 and did not have complaints indicating intestinal lesions.

Among the examined patients of group I, there were 64 (61.5 %) men and 40 (38.5 %) women. The average age was (54.3 ± 6.1) years. Among the patients of group II, there were 47 (60.3 %) men and 31 (39.7 %) women. The average age was (52.4 ± 5.7) years. The control group included 20 practically healthy individuals: 12 men (60.0 %), and 8 women (40.0 %). The average age was (51.4 ± 4.6) years.

The exclusion criteria were a positive test for SARS-CoV-2 RNA at the time of the study; a positive test for *Clostridium difficile* antigens in the feces; the presence of alcoholic, autoimmune, viral (hepatitis B, C, D viruses) liver damage; ulcerative colitis, Crohn's disease in history; lactose intolerance, gluten intolerance.

All studies were performed with the consent of the patients (written consent was obtained from all patients for the relevant diagnostic and treatment measures), and the methodology was in line with the Helsinki Declaration of Human Rights of 1975 and its revision of 1983, the Council of Europe Convention on Human Rights and Biomedicine, and the legislation of Ukraine.

All examined patients were subjected to general clinical, anthropometric, instrumental, and laboratory methods. To verify the diagnosis, attention was paid to the nature of the complaints and the history of the disease. During the anthropometric examination, height, weight, and waist circumference were determined, and body mass index (BMI) was calculated. According to WHO recommendations, patients were divided according to BMI, with a BMI of 16.0 kg/m^2 or less corresponding to severe underweight; 16.0–18.5 kg/m^2 — to underweight; 18.0–24.9 kg/m^2 — to normal weight; 25.0–29.9 kg/m^2 — to overweight; 30.0–34.9 kg/m^2 — to obesity of the first degree; 35.0–39.9 kg/m^2 — to obesity of the second degree; 40.0 kg/m^2 and more — to obesity of the third degree [7].

Standard general and biochemical tests were performed in the blood serum to determine the functional state of the liver, lipid, and carbohydrate metabolism. All patients underwent an ultrasound examination of the abdominal cavity according to the conventional method. All patients of group I underwent endoscopic examination of the colon (EC) according to the generally accepted methodology using a Pentax EC-380LKp video colonoscope (Japan), which assessed the state of the mucous membrane (MM) of the EC (determined the state of the intestinal lumen, its tone, the severity of folds, vascular pattern, hyperemia, swelling of the TC MU and contact bleeding, presence of looseness, the granularity of the MU, presence of defects in the MU and hemorrhages, polypoid formations (pseudopolyps), diverticula). The examination was performed under general anesthesia. Biopsy material from different parts of the intestine was also taken from all patients for histological examination.

The diagnosis of NAFLD was made according to the criteria of the unified clinical protocol (Order of the Ministry of Health of Ukraine of 06.11.2014, No. 826) and the EASL-EASD-EASO guidelines for the diagnosis and treatment of NAFLD [8]. The degree of liver damage was determined using surrogate markers of fibrosis with the help of online calculators NAFLD fibrosis score, Fibrosis 4 calculator (FIB-4), fibrotest, and liver elastometry results.

Serum levels of neurokinin B (NK-B) were measured by enzyme-linked immunosorbent assay (ELISA) using a test system from Wuhan Fine Biotech Co., Ltd.

The analysis and processing of the results of the examination of patients was carried out using the computer program Statistics for Windows v.10.0 (StatSoft Inc., USA) using parametric and nonparametric methods of evaluating the results obtained.

Results

Intestinal complaints in patients with NAFLD of group I on average occurred (6.2 ± 1.4) months after COVID-19.

Complaints indicating intestinal lesions in patients with NAFLD after COVID-19 were more often manifested by changes in the act of defecation, namely constipation was diagnosed in 51.0 % of the subjects ($p < 0.001$), a tendency to diarrhea was determined in 26.9 % of patients, and in 22.1 % of patients in group I constipation followed by diarrhea was diagnosed (Table 1).

A significant proportion of patients in group I had flatulence (up to 81.7 %), as well as pain along the colon and a feeling of incomplete emptying. It should be noted that in group II patients, 19.2 % of patients had flatulence and 12.8 % of patients had alternating constipation and diarrhea.

The anthropometric examination revealed overweight and obesity of the first degree more often in patients of both groups, with overweight and obesity of the first degree most often diagnosed in patients of group I (38.5 % of the examined), while in patients of group II — overweight (42.3 % of patients, respectively; $p < 0.05$) (Table 2).

All patients of both groups under our observation were diagnosed with NAFLD, namely, non-alcoholic steatohepatitis of minimal activity (Table 3).

As indicated by the results of the data obtained, patients in both groups showed laboratory signs of cytolytic syndrome (increased activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST)), as well as cholestatic syndrome, which was manifested by an increase in the level of total bilirubin (TB), alkaline phosphatase (ALP) and gamma-glutamyl transaminase (GGT) in the blood serum.

The level of neurokinin B in the blood serum of the examined patients with NAFLD was determined (Table 4).

Table 1 — Clinical manifestations of intestinal lesions in the examined patients, %

Clinical manifestation	Patients with NAFLD examined	
	Group I (n = 104)	Group II (n = 78)
Constipation	51.0**	9.0
Diarrhea	26.9	–
Constipation followed by diarrhea	22.1*	12.8
Flatulence	81.7**	19.2
Pain in the colon	57.0	–
Feeling of incomplete bowel movement	40.4	–

Note. The difference between the indicators in patients by groups is significant: * — p < 0.05; ** — p < 0.001.

Table 2 — Distribution of examined patients with NAFLD depending on BMI, %

Indicator	Patients examined	
	Group I (n = 104)	Group II (n = 78)
Normal weight (BMI: 18.0–24.9)	8.7	11.5
Overweight (BMI: 25.0–29.9)	28.8	42.3*
Obesity of the first degree (BMI: 30.0–34.9)	38.5*	25.7
Obesity of the second stage (BMI: 35.0–39.9)	19.2	19.2
Obesity of the third degree (BMI: more than 40.0)	4.8	1.3

Note. The differences between the indicators in patients of groups I and II are significant: * — p < 0.05.

Table 3 — Indicators of the functional state of the liver in the subjects

Indicator	Control group (n = 20)	Patients examined	
		Group I (n = 104)	Group II (n = 78)
ALT, U/l	20.3 ± 1.3	104.1 ± 2.8***	94.8 ± 3.0**
AST, U/l	18.7 ± 0.9	82.3 ± 3.0**	69.5 ± 2.7**
TB, mmol/l	14.5 ± 0.8	28.7 ± 1.6*	29.3 ± 1.4*
ALP, mmol/l	70.9 ± 2.1	142.9 ± 2.4**	144.7 ± 2.0**
GGT, U/l	34.7 ± 1.8	88.0 ± 2.2*	74.6 ± 2.5**

Note. The difference between the indicators of the control group and the examined patients of groups I and II is statistically significant: * — p < 0.05; ** — p < 0.01; *** — p < 0.001.

Table 4 — Serum neurokinin B levels in the subjects

Indicator	Control group (n = 20)	Patients examined	
		Group I (n = 104)	Group II (n = 78)
NK-B, pg/ml	0.286 ± 0.007	0.857 ± 0.016**+	0.310 ± 0.011*

Note. The difference between the indicators of the control group and the examined patients of groups I and II is statistically significant: * — p < 0.05; ** — p < 0.001; between the indicators of patients of groups I and II the difference is statistically significant: + — p < 0.01.

A significant increase in serum NK-B levels in patients with NAFLD with minimal deviations from the norm in patients of group II (1.1-fold; $p < 0.05$) was found, while in patients of group I significant deviations from the norm were diagnosed (3.0-fold; $p < 0.001$).

To determine the possible role of NK-B in the formation of clinical changes in the intestine in patients with NAFLD, especially in COVID-19, we analyzed its level depending on the violation of the defecation act in these patients (Table 5).

According to the data obtained, in patients with NAFLD after COVID-19 (group I), the lowest levels of NK-B were diagnosed in intestinal damage manifested by constipation. Also, in patients of group II with NAFLD, who complained of periodic constipation, a tendency to decrease the level of this neuropeptide in the blood serum was determined. In patients with diarrhea in NAFLD after COVID-19, the level of NK-B was maximal and 6.2 times ($p < 0.001$) higher than in the control group. In patients with constipation followed by diarrhea, an increase of 1.6 and 1.2 times (in patients of groups I and II, respectively) was determined compared with the control group.

A statistical analysis was performed to determine the relationship between the level of NK-B in the blood serum and the index of liver function, BMI, and clinical signs of intestinal damage in the subjects (Table 6).

The correlation analysis made it possible to establish a direct relationship between the level of NK-B, depending on the predominance of the clinical variant of the defecation disorder, and the severity of pain along the colon and a feeling of incomplete bowel movement, mainly in the subjects of group I. According to the data obtained, the level of NK-B in the blood serum directly depends on the severity of BMI disorders in both groups of patients with NAFLD. Flatulence in patients with NAFLD also depends on the level of neurokinin B in the blood serum. The analysis shows an inverse relationship between neurokinin B and ALT activity in these patients.

Thus, our studies allowed us to establish abnormalities in the level of non-neurotransmitter (neurokinin B) in the blood serum of patients with NAFLD in the setting of post-COVID-19 lesions. The data obtained indicate the dynamics of its level depending on the clinical form of intestinal damage. The data also suggest that changes in neuromodulators may be one of the reasons for the formation of clinical manifestations of intestinal damage in patients with NAFLD after COVID-19.

Discussion

Proper performance of the motor and absorptive functions of the colon requires optimal implementation of central and local nervous and humoral mechanisms of contractile activity of the smooth muscles of its wall. Disorders in the regulation of colon motor activity can be etiological factors in the occurrence of such pathological phenomena as irritable bowel syndrome, diarrhea, constipation, etc. However, the study of the morphological and physiological aspects of the correction of colon motor function is still far from perfect and requires the emergence of comprehensive fundamental research on this issue.

Colonic motility is a complex set of mechanisms involving several levels of nervous and humoral regulation, ranging from local metasympathetic and paracrine influences

Table 5 — Serum neurokinin B levels in patients depending on clinical manifestations of intestinal lesions, pg/ml

Clinical manifestation	Patients examined	
	Group I (n = 104)	Group II (n = 78)
Constipation	0.173 ± 0.009	0.215 ± 0.010*
Diarrhea	1.782 ± 0.023#	–
Constipation followed by diarrhea	0.446 ± 0.014++	0.333 ± 0.011^+

Note. The difference between the indices in patients of groups I and II with constipation is statistically significant: * — p < 0.05; the difference between the indices in patients of groups I and II with constipation followed by diarrhea is statistically significant: ^ — p < 0.01; between the indicators in patients of group I with constipation and diarrhea, the difference is statistically significant: # — p < 0.001; between the indicators in patients of groups I and II with constipation and constipation followed by diarrhea, the difference is statistically significant: + — p < 0.05; ++ — p < 0.01.

Table 6 — Comparison of NK-B levels with clinical and laboratory parameters in the examined patients

Indicator	Group I			Group II	
	Constipation	Diarrhea	Constipation followed by diarrhea	Constipation	Constipation followed by diarrhea
ALT	r = –0.78; p < 0.01	r = –0.66; p < 0.05	r = –0.74; p < 0.05	r = –0.50; p < 0.05	r = –0.44; p < 0.05
BMI (overweight)	r = 0.80; p < 0.01	–	r = 0.78; p < 0.01	r = 0.68; p < 0.05	–
BMI (grade I obesity)	r = 0.92; p < 0.01	r = 0.82; p < 0.01	r = 0.80; p < 0.01	–	–
Flatulence	r = 0.72; p < 0.05	r = 0.70; p < 0.05	r = 0.74; p < 0.05	r = 0.64; p < 0.05	r = 0.56; p < 0.05
Pain in the colon	r = 0.92; p < 0.01	r = 0.90; p < 0.01	r = 0.90; p < 0.01	–	–
The feeling of an incomplete bowel movement	r = 0.86; p < 0.01	r = 0.78; p < 0.01	r = 0.92; p < 0.01	–	–

to central regulatory effects. Nervous influences, which are realized through extra-organic nerves and through the implementation of metasympathetic enteric motor reflexes, are combined with numerous and complex humoral effects. The cholinergic system, as well as purines and some regulatory peptides, have a stimulatory effect on intestinal propulsion, while serotonergic, tachykinergic, and sympathetic effects play a modulating role in this complex neurohumoral regulatory process. The endpoint of the regulation of intestinal motility is the release of acetylcholine by cholinergic excitatory motoneurons and the release of nitric oxide and VIP by non-adrenergic noncholinergic inhibitory motoneurons. It has been established that the contractile activity of colonic smooth muscle cells is determined by a complex of interrelated central and local nervous influences, as well as intestinal neurotransmitters, neuromodulators, and hormones of the adrenergic, purinergic, nitrergic, peptidergic, cholinergic, serotonergic and other systems [9, 10].

Motor activity in the colon is largely determined by the localization of enteric neurons and peptide neurotransmitters. Nitric oxide and neuropeptide Y-secreting neurons project caudally as interneurons or as inhibitory motor neurons innervating circular smooth muscle. Sympathetic preganglionic neurons, along with acetylcholine, also release the peptides enkephalin and neurotensin from their axonal endings. Parasympathetic preganglionic neurons secrete enkephalin and acetylcholine, and postganglionic neurons secrete enkephalin, VIP, and acetylcholine. One-third of myenteric neurons, along with acetylcholine, contain tachykinin-substance P and neurokinin A. In some neurons of the myenteric plexus, somatostatin, and opioid peptides are involved as neuro-neuronal modulators in neuronal circuits involving interneurons.

Tachykinins, which consist of three types of peptides (substance P, neurokinins A and B), bind to the corresponding receptors on smooth muscle cells, modulating their motor activity. The main effect of Substance P and other tachykinins is to stimulate the contractile activity of the gastrointestinal tract, which is typical for almost all parts of the mammalian digestive tract. Substance P, along with acetylcholine, is one of the main neurotransmitters released by excitatory motor neurons during muscle contraction. Endogenous substance P and neurokinin-A interact with other enteric transmitters in the physiological control of gastrointestinal motor activity. Tachykinergic pathways are involved in the stimulation of 5-HT4 receptor agonists in the motor activity of the digestive tract. That is, there is a synergistic effect of the peptidergic and serotonergic systems in the regulation of the muscular activity of the digestive tract.

Tachykinins can inhibit motor activity by stimulating inhibitory neuronal pathways or blocking stimulatory ones. The intestinal mucosa contains a population of enterochromaffin cells that synthesize and secrete substance P and enkephalins along with serotonin. It is believed that serotonin, by causing the development of slow excitatory postsynaptic potentials in the network of neurons containing substance P, ensures synchronous contraction/relaxation of the intestinal wall. Serotonergic neurons are thus triggers of coordinated muscle activity, which, in turn, is ensured by the excitation of multipolar SP neurons. Enkephalins, by reducing the excitability of myenteric plexus neurons, serve as a counterbalance to serotonin — they block its stimulating effect on neurons containing the substance P [9].

At the same time, there is a lack of literature on the importance of neuropeptides in the mechanisms of colon lesions, especially in patients with NAFLD after COVID-19. There are also only a few publications, mostly of an experimental nature, on the possibilities of using neuropeptide analogues to correct the detected changes in these signaling molecules in certain chronic digestive diseases.

Both experimental and clinical studies on the role of NK-B in the body are primarily conducted in diseases of the genital area (puberty, participation in the progression of clinical manifestations of menopause in women, etc).

Our results suggest the influence of changes in serum NK-B levels in the formation and progression of bowel lesions in patients with NAFLD after COVID-19. At the same time, a decrease in NK-B levels is associated with constipation, which is probably due to a decrease in colonic contractile activity against the background of changes in its neuroendocrine regulation. On the contrary, high levels of this neurotransmitter in patients with NAFLD with NK-B diarrhea are associated with its participation in the acceleration of intestinal peristaltic waves in these patients.

However, further studies are needed to better understand the impact of neurokinin B alterations on the formation and progression of intestinal lesions in patients with NAFLD after COVID-19.

Conclusions

1. In patients with NAFLD, intestinal damage after COVID-19 is more often manifested by constipation (in 51.0 % of cases).

2. In patients with NAFLD after COVID-19, changes in the level of neurokinin B in the blood serum were found, with its minimum values found in patients with constipation ((0.173 ± 0.009) pg/ml; $p < 0.01$), and maximum values were diagnosed in patients with diarrhea (its increase to (1.782 ± 0.023) pg/ml; $p < 0.001$).

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Authors' contribution. *Sirchak Ye.S.* — concept and design of the study, analysis of the data; *Stehura A.V.* — selection of cases for the analysis, processing of the material, and text presentation.

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Рівень нейрокініну В у пацієнтів із неалкогольною жировою хворобою печінки та ураженням кишечника після COVID-19

Резюме. ***Актуальність.*** Дослідження нейропептидів, у тому числі субстанції Р, нейрокінінів, може виявити ймовірні механізми прогресування уражень шлунково-кишкового тракту із формуванням його моторної дисфункції в осіб із коронавірусною хворобою 2019 (COVID-19), особливо при метаболічно асоційованих станах, таких як неалкогольна жирова хвороба печінки (НАЖХП), ожиріння, цукровий діабет 2 типу. ***Мета:*** визначити особливості зміни рівня нейрокініну В (NK-B) у сироватці крові пацієнтів із НАЖХП після COVID-19. ***Матеріали та методи.*** У наукове дослідження включено 104 особи з НАЖХП та ураженням кишечника на амбулаторному етапі спостереження після COVID-19 (вони ввійшли в основну, I групу обстежених). У II групу (порівняння) включено 78 пацієнтів із НАЖХП, які не хворіли на COVID-19, а також не мали скарг, що вказують на ураження кишечника. В усіх обстежених визначали рівень NK-B у сироватці крові. ***Результати.*** Скарги, що вказували на ураження кишечника в осіб із НАЖХП після COVID-19, частіше проявлялись зміною акту дефекації, а саме: запори діагностовано в 51,0 % випадків ($p < 0,001$), схильність до діареї — у 26,9 %, а в 22,1 % обстежених I групи виявлено запори, що змінюються проносами. При НАЖХП установлено вірогідне збільшення сироваткового рівня NK-B із мінімальними відхиленнями від норми у пацієнтів II групи (в 1,1 раза; $p < 0,05$), тоді як у I групи зареєстровано суттєві відхилення від норми (у 3,0 раза; $p < 0,001$). При ураженні кишечника, що проявляється запорами, показники NK-B були найменшими. У пацієнтів із діареєю на тлі НАЖХП після COVID-19 рівень NK-B був максимальним і в 6,2 раза ($p < 0,001$) перевищував показники контрольної групи. ***Висновки.*** В обстежених із НАЖХП ураження кишечника після COVID-19 частіше проявляється запорами (51,0 % випадків). У пацієнтів із НАЖХП після COVID-19 встановлено зміни рівня нейрокініну В у сироватці крові, при цьому мінімальним він був у хворих із запорами ($(0,173 \pm 0,009)$ нг/мл; $p < 0,01$), а максимальним — в осіб із діареєю (збільшення до $(1,782 \pm 0,023)$ нг/мл; $p < 0,001$).

Ключові слова: неалкогольна жирова хвороба печінки; ураження кишечника; COVID-19; нейрокінін В