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HELICOBACTER PYLORI INFECTION AND NON-ALCOHOLIC FATTY LIVER DISEASE IN THE WORKING POPULATION OF SOUTH YAKUTIA: ASSOCIATION RESEARCH

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A one-time study of the working population of non-indigenous nationality in the southern zone of Yakutia was carried out. A total of 78 people were analyzed, including 31 men, Me age 45.0 [35.0-54.0] years, and 47 women, Me - 43.5 [36.0-53.0] years. A high incidence of Helicobacter pylori infection was found, regardless of comorbidity. The association of HP infection with body mass index, waist circumference, lipid spectrum disorders and metabolic syndrome according to IDF 2005 criteria was not obtained (p>0.05). In the course of the study, the relationship between NAFLD and infection with Helicobacter pylori infection was not obtained (p>0.05).

Keywords: Helicobacter pylori infection, obesity, non-alcoholic fatty liver disease, non-indigenous population, Yakutia.

There is a steady increase in the spread of non-alcoholic fatty liver disease (NAFLD) in the world, along with obesity and metabolic syndrome. Metabolic disorders in addition to metabolic syndrome, insulin resistance, type 2 diabetes mellitus includes NAFLD. The development of both metabolic syndrome and NAFLD is often based on insulin resistance, leading to disorders of lipid, carbohydrate and fat metabolism, the release of free fatty acids and the accumulation of fat and an inflammatory reaction in the liver. It has been proven that NAFLD is an independent predictor of the development of malignant tumors, including hepatocellular carcinoma [4; 10; 13]. In patients, one of the risk factors for NAFLD is increased permeability of the intestinal wall caused by excessive bacterial growth and the action of endotoxins (lipopolysaccharides). The influence of *Helicobacter pylori* (HP) on the development and course of gastritis, peptic ulcer and stomach cancer is evident, but in recent years there has been an assumption about its systemic effect on many different organs, special attention is paid to the contribution to the development of metabolic syndrome and NAFLD. But the evidence is few and mostly contradictory. Some researchers have proved that HP–infected individuals had a more unfavorable metabolic profile, increased body mass index (BMI), blood pressure (BP), triglyceride level (TG) and the highest prevalence of NAFLD [7; 8; 11; 16]. Other studies have not revealed a connection between them [12; 14; 15]. Previously, studies were conducted on the non-indigenous population of South Yakutia, where the highest frequency of pathology of the digestive, cardiovascular and endocrine systems was revealed [3]. Given the high frequency of detection of digestive diseases in this contingent, as well as the few studies of the effect of *Helicobacter pylori* on the development of NAFLD, the relevance of our study is beyond doubt.

The aim of the study: identify the association of HP infection with the development of non-alcoholic fatty liver disease in the working population of non-indigenous nationality living in south Yakutia.

Materials and methods of research. A pilot cross-sectional study of 78 industrial and social workers in the southern zone of Yakutia was conducted. All were representatives of non-indigenous nationality, including 31 men, whose median (Me) age was 45.0 [35.0-54.0] years, and 47 women, Me age 43.5 [36.0-53.0] years.

All study participants were surveyed, their complaints and anamnesis were taken, anthropometric study with the

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determination of height, body weight, measurement of waist circumference (WC) and hips, measurement of blood pressure (BP) were conducted, their blood was taken from the ulnar vein in the morning on an empty stomach with an 8-12-hour interval after the last meal, a clinical examination by a physician was also conducted. The voluntary consent of the participants to the study was a prerequisite, according to the Protocol of the local Ethics Committee of the YSC CMP.

In order to detect abdominal obesity, a measurement was performed from a standing position, patients wearing only underwear. The measurement point is the midpoint of the distance between the top of the iliac crest and the lower lateral edge of the ribs. It does not necessarily have to be at the navel level. At > 94 cm in men and > 80 cm in women, it can be assumed that the patient has abdominal type of obesity (IDF criteria 2005, RSC 2009).

Blood pressure was measured twice with an automatic tonometer "OMRON M2 Basic" (Japan) in a sitting position with the calculation of average blood pressure with a limit of permissible measurement error of ± 3 mm Hg (ESH/ESC, 2013). Arterial hypertension (AH) was assumed at a blood pressure level≥140/90 mmHg or if the patient was taking antihypertensive drugs during the examination period (ACC/AHA Guideline, 2017).

Laboratory analyses were carried out by the enzymatic method on an automatic biochemical analyzer "Labio" using "Analyticon" reagents (Germany). Laboratory research methods included: determination of the lipid spectrum (total cholesterol (TC), low-density lipoprotein cholesterol (LDL cholesterol), high-density lipoprotein cholesterol (HDL cholesterol), TG) and glucose. The enzyme immunoassay included the determination of total antibodies to the *CagA Helicobacter pylori* antigen in blood serum on the Uniplan enzyme immunoassay analyzer using "Vector-Best" reagents.

The diagnosis of "Non-alcoholic fatty liver disease" was made on the basis of an ultrasound examination of the liver on an empty stomach and the conclusion of a general practitioner. The exceptions were alcoholic liver damage, chronic viral hepatitis and cirrhosis.

Metabolic syndrome (MS) was assessed according to the criteria of the IDF (International Diabetes Federation) 2005: the presence of the main component - abdominal obesity (in men from ≥94 cm and in women from ≥ 80 cm) and two other criteria from the listed options: blood pressure≥140/90 mmHg, fasting glucose > 5.8 mmol/l or type 2 diabetes mellitus, TG>1.7 mmol/l (>150 mg/dl), HDL cholesterol in men <1.0 mmol/l (<40mg/dl), in women <1.1 mol/l (<50mg/dl).

Statistical analysis was carried out using the SPSS STATISTICS software package (version 26.0). Qualitative variables are described by absolute and relative frequencies (%), quantitative variables are described using the mean and standard error of the mean, median (Me) and interquartile range (Q1-Q3). The share comparison of the groups was carried out using the nonparametric Spearman criterion χ2. The odds ratio (OR) and 95% confidence interval (95% CI) were calculated. The correlation analysis was carried out using the Spearman coefficient. The statistical significance of the differences (p) was less than 5%.

The work was carried out under the research project of the YSC CMP "Regional peculiarities of biochemical, immunological and morphological indicators in the indigenous and non-indigenous population of the Republic of Sakha (Yakutia) in normal conditions and pathology" (FGWU-2022-0014) and the research of the Academy of Sciences of the Republic of Sakha (Yakutia) "Assessment of radiation exposure of the population of the Aldansky district due to natural sources of radiation and recommendations for carrying out protective measures to reduce it."

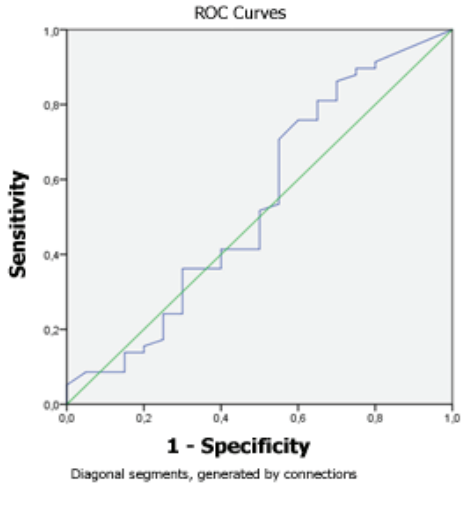
Research results and discussion. The conducted study for the presence of antibodies to the Helicobacter Pylori antigen in the non-indigenous population of South Yakutia revealed that more than half of the examined individuals (n=60 or 76.9%) had positive antibody tests, 24 out of 31 men (77.4%) and 36 women (76.6% of all women) without a significant difference (p>0.05).

We analyzed the relationship of HP infection with anthropometric parameters (BMI, WC). For this purpose, two groups were identified: HP-positive (or main) group (60 people) and HP-negative (control) group (18 people). The average titer of antibodies to Helicobacter Pylori was 4.39±0.31 cu in the main group, 0.35±0.22 cu in the control group with a significant difference (p=0.000).

As a result of statistical analysis, it was found that 35% of the main group (n=21) were overweight, obesity was found in 20 people, or 33.3%. In the group without infection, overweight was registered in 16.7% (n=3), obesity in 61.1% (n=11). We did not obtain statistically significant differences between the groups in the frequency of occurrence of overweight and obesity by BMI (χ^2=3.76, p=0.052). A comparative analysis of the frequency of occurrence of AO revealed a high frequency regardless of the presence of infection. Thus, in the main group, 65.5% (n=40) had AO, in the control group 82.3% (n=14), there were no significant differences (p=0.370). A correlation analysis of HP infection with anthropometric data was further carried out, resulting in a negative correlation with BMI (r=-0.204,

The correlation of *Helicobacter pylori* with the lipid spectrum

Parameter	TG	TC	HDL cholesterol	LDLcholesterol
r	- 0.174	- 0.077	0.073	- 0.050
p	0.127	0.503	0.525	0.664



Model: NAFLD- no and NAFLD- yes
Variables: HP antibody titer
NAFLD prognosis 1 – positive;
0- negative
N=78

ROC-titer curve of antibodies to *Helicobacter pylori* in relation to the development of NAFLD

p=0.073) and WC (r=-0.088, p=0.444).

Thus, the conjugacy of HP infection with BMI was not obtained (p0,05). The high incidence of obesity is due to the general prevalence in the population.

To identify the association of HP infection with systolic blood pressure, a correlation analysis was performed, during which a negative insignificant correlation was obtained (r= -0.062, p=0.589).

The relationship between the presence of *Helicobacter pylori* and MS according to the criteria of the IDF 2005 was also not revealed. Thus, 21 people or 35% of the HP-positive group (OR 1,122 [95% CI: 0.863-1.459]) and 8 people (47%) of the HP-negative group (OR 0.680 [95% CI: 0.295-1.564]) had MS (χ^2=0.820, p=0.365).

The correlation of HP infection with blood biochemical parameters, in particular with the lipid spectrum, was analyzed (Table 1). The table clearly shows the absence of a significant correlation of infection with lipid indicators with some negative association.

Thus, the association of HP infection with lipid metabolism disorders, blood pressure, MS in the non-indigenous population of South Yakutia has not been revealed.

Of all the examined persons, 25.6% (n=20) were diagnosed with NAFLD, of which 10 were men (32.3%) and 10 were women 21.3% (χ2=1.18, p=0.277). Our data on the frequency of NAFLD detection are consistent with many studies of scientists [1; 6; 9]. The analysis of the relationship of NAFLD with the biochemical parameters of blood, in particular with the lipid spectrum, was carried out. The association was revealed only with an increased level of TG, the odds ratio was 3.079 ([95%CI: 1.078-8.792], p=0.032). With other indicators of lipid metabolism: increased levels of TC, LDL cholesterol, reduced HDL conjugacy was not obtained (OR 1.310 [95%CI: 0.472-3.633], p=0.604; OR 0.741 [95%CI: 0.233-2.351], p=0.424; OR 0.500 [95%CI: 0.119-2.109], p=0.424).

AO (100%) was found in all patients with NAFLD, thereby confirming the close association of obesity with the development of NAFLD, confirming its higher prevalence among patients with NAFLD, 75-93% [2; 5]. Taking into account the overall picture of the scale of the obesity epidemic in the world, the "control" also revealed a high incidence of AO, detected in 34 people, which was 58.6% (χ2=11.95, p=0.000). An analysis of the conjugacy with the level of systolic blood pressure was also carried out, during which no statistically significant correlation with NAFLD was obtained (r=0.201, p=0.078).

The incidence of NAFLD in the HP-positive group was 23.3% (n=14), in the HP-negative 33.3% (n=6), with no significant difference (OR 0.55 [95%CI: 0.17-1.87], p=0.302).

For the prognostic significance of *Helicobacter pylori* in relation to the risk of developing NAFLD, we additionally performed an ROC analysis (Fig.1).

To determine the significance, an ROC curve was plotted on a square diagram for each biomarker, a threshold cut-off point was determined with maximum specificity and sensitivity of the test when using it, as well as the area under the ROC curve - AUC (AreaUnderCurve). We selected a threshold point value of 4,135 cu with a sensitivity of 43.1% and a specificity of 50.0%. The area under the ROC curve – AUC of the antibody titer was 53.8% (0.538), (95% CI 0.378-0.698), p=0.081. According to the analysis, we can conclude a negative diagnostic significance of the antibody titer index for *Helicobacter pylori* in the development of NAFLD.

Conclusion. Thus, in our pilot study, the relationship of NAFLD with helicobacter infection was not obtained, possibly due to a small sample size. Nevertheless, we have confirmed the research results of a number of foreign authors [12; 14; 15]. A high incidence of *Helicobacter pylori* infection was revealed in the working population of non-indigenous nationality of South Yakutia, regardless of concomitant pathology. Mandatory eradication of HP infection with subsequent serological examination or fecal analysis for the *Helicobacter pylori* antigen is recommended for all patients of the positive group, taking into account its direct impact on the development of pathology of the gastroduodenal system, in particular gastric ulcer and duodenal ulcer, as well as stomach cancer. Patients with NAFLD are recommended to regularly conduct ultrasound examination of the liver, pathogenetic treatment, commit to weight loss, follow a balanced hypocaloric nutrition and comply with the principles of a healthy lifestyle.

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THE LEVEL OF ENDOGENOUS INTOXICATION IN OVERWEIGHT INDIVIDUALS

According to the data obtained, there is an increase in the levels of low and medium molecular weight substances and oligopeptides in plasma, erythrocytes, and urine, depending on body weight. In obese individuals, there was a significant increase in the concentrations of low and medium molecular weight substances and oligopeptides compared to those with normal body weight in all biological samples studied, indicating endogenous intoxication in the body of obese individuals.

Keywords: low and medium molecular weight substances, oligopeptides, obesity, overweight, endogenous intoxication.

Introduction. At present, the problem of obesity is urgent both worldwide and in Russia [5]. Modern man is exposed to several factors leading to obesity (abundance and caloric content of food, hypodynamia, psycho-emotional-stresses, bad habits, and ecology).

Obesity leads to serious complications in human health. People suffering from obesity are more prone to the development of cancer [6, 13], cardiovascular [9], autoimmune diseases [11]. Obesity is a risk factor for severe outcomes in COVID-19 disease [8]. In addition, obesity is the cause of leading a person to disability and death [5].

Obesity is a complex, multifactorial disease, the development of which, along with genetic predisposition, is greatly influenced by external factors that lead to metabolic disorders in the human body. Disturbance of metabolic processes leads to endogenous intoxication (EI) development. According to many authors, EI is a nonspecific process in diseases of different etiology, pathogenesis, and severity [1]. In patients with chronic EI, there is often a shift in homeostasis, leading to decreased body resistance [10, 12].

In connection with those mentioned above, detection EI in risk groups for correction of this condition is an urgent task. In scientific and clinical studies, the determination of low and medium molecular weight substances (LMMWSs) as markers of EI is widespread.

There have been no studies on the level of LMMWSs as markers of EI in overweight and obese residents of Yakutia.

Materials and methods. The present work was carried out in the Yakut Science Centre of Complex Medical Problems under the research work: "Regional characteristics of biochemical and immunological parameters in the indigenous and native population of the Republic of Sakha (Yakutia) in norm and pathology". The material was collected during medical and biological expeditions during the health examination of the population of Yakutia in the spring period from 2015 to 2019. It was mandatory to obtain informed consent of the respondents for the study (according to the protocol of the Ethical Committee of Yakut Science Centre of Complex Medical Problems №49 dated 25.03.2018).

Fifty people aged 31 to 50 years were examined. The body mass index (BMI) = m (kg) / h^2 (m), where m-body weight, h-height, was calculated for each individual. According to the BMI, the examined persons were divided into three groups: the first group included 15 people with normal body weight (BMI from 18 to 24.9), the second group included 20 people with overweight (BMI from 25 to 29.9) and the third group included 15 obese people (BMI from 30 and above). The study material was blood from the ulnar vein on an empty stomach.

The content of LMMWSs estimated the level of EI according to the method of M.Y. Malakhova [7]. The determination of oligopeptides (OPs) was evaluated using the Lowry protein assay. In plasma, blood erythrocytes, and urine we calculated the coefficients of the complex assessment of endotoxemia: K1 - ratio of LMMWSs concentration in plasma to LMMWSs concentration in erythrocytes; K2 - ratio of LMMWSs concentration in urine to the sum of LMMWSs concentrations in blood plasma and erythrocytes; K3 - ratio of oligopeptide (OPs) concentration in urine to the sum of OPs concentrations in blood plasma and erythrocytes.

Biochemical parameters were studied in serum. The concentrations of cholesterol, triglycerides, high-density lipoproteins, glucose, alanine aminotransferase and aspartate aminotransferase were determined on an automatic biochemical analyzer Chem Well 2902.

The obtained data was performed using IBM SPSS Statistics 19 program. In this article, quantitative indicators are presented in the format Mean ± SD, where Mean is the arithmetic mean, and SD is the error of the arithmetic mean.

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