

**G.R. Bikbavova*¹, M.A. Livzan², V.I. Sovalkin¹,
D.V. Turchaninov³, O.E. Lopatina¹, T.V. Tretyakova⁴,
A.P. Ahramovich⁴, T.S. Gordienko⁵**

¹ — Omsk State Medical University, General Medicine, Advanced Course, and Endocrinology Department, Omsk, Russia

² — Omsk State Medical University, General Medicine, Intermediate Course, and Occupational Diseases Department, Omsk, Russia

³ — Omsk State Medical University, Hygiene and Human Nutrition Department, Omsk, Russia

⁴ — Omsk Regional Clinical Hospital, Omsk, Russia

⁵ — Omsk Clinical Diagnostic Center, Omsk, Russia

MODERN LIFESTYLE AND ITS IMPACT ON THE ULCERATIVE COLITIS INCIDENCE

Abstract

The objective of the study: To assess the significance of surrogate markers of the «hygiene hypothesis», the «old friends' theory» and the hypothesis of «depletion of biomes» in the development of ulcerative colitis among the population of Western Siberia. **Materials and methods:** An active survey (interviewing) of 81 patients with ulcerative colitis and 39 healthy respondents was conducted. The main surrogate markers of the «hygiene theory», the hypotheses of «old friends» and «depletion of biomes» were studied: past infestations, pets in childhood, use of antibiotics, breastfeeding, family size (number of siblings), attendance at pre-school institutions, accommodation in a dormitory while studying, accommodation in a city or a village, type of drinking water supply and the type of water respondents use for drinking; in the framework of the «biome depletion» theory, in addition to the markers listed above, a sugar consumption rate was assessed. Consumption of simple carbohydrates was calculated based on the number of cups of tea and/or coffee drunk per week and the number of teaspoons or cubes of sugar that the respondent puts in one cup. **Results.** Among the indirect markers of the «hygiene hypothesis» and the theory of «old friends» examined, only one effect the risk of ulcerative colitis among the population of the Omsk region — visiting preschool institutions ($ZI = 4.59$, $p < 0.05$). Of the indirect signs of the «biome depletion» hypothesis examined, significant differences were found in the amount of simple carbohydrates consumed: patients with ulcerative colitis had consumed more sugar with tea and/or coffee in the period before the first signs of the disease than healthy respondents ($U = 1214.0$; $Z = 2.0$; $p = 0.04$). **Conclusion.** In our study, the statistical significance of such factors as rare visits to kindergartens and the consumption of large amount of sugar by patients with ulcerative colitis in the period before the onset of the disease in comparison with healthy respondents was demonstrated.

Key words: *ulcerative colitis, «hygiene hypothesis», the hypothesis of «depletion of biomes»*

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IBD — inflammatory bowel disease, UC — ulcerative colitis

* Contacts. E-mail: galiya1976@mail.ru

Introduction

The main theory of the pathogenesis of inflammatory bowel diseases (IBD) is currently considered a disorder of immune regulation and activation of immune response against antigens of the intestinal microflora in genetically predisposed individuals under the influence of certain environmental factors. According to some scientists [1], the epidemiological trend towards the increase in IBD prevalence is associated with the improvement of the general hygienic conditions of modern society. One of the theories explaining the increase in autoimmune disease and various allergic reactions is the «hygiene hypothesis», which was articulated by David Strachan, an English epidemiologist [2]. This theory considers the influence of family size at an early age, attendance at preschool institutions and the presence of pets in childhood, living in a childhood with siblings that involves more contact with different microorganisms [3]. In contrast, the use of centralized water supply, filters for everyday needs, antibacterial wipes, soap, dishwashing detergents leads to a decrease in the antigenic effect on the body in childhood, which can be the cause of an excessive immune response in contact with microbes in adulthood. The rapid elimination of bacteria with antibiotics and modern hygiene products with antibacterial action makes it impossible to form an individual's own immunity against infections.

In 2003, Graham Rook proposed the hypothesis of «old friends» [4], the essence of which is that not only bacterial infections, but also infestations that occurred in childhood, play an important role in the formation of immunity. The difference of this theory from the «hygiene hypothesis» is that not all antigens of the environment are important for the harmonious development of immune mechanisms, but rather microorganisms and parasites («old friends») with low pathogenicity. Russian and foreign researchers consider [5] the «hygiene theory» and «old friends' theory» as contradictory, and their confirmation requires adequately designed studies. According to researchers, the first years of life have a special impact on the risk of autoimmune diseases. If during this period a child spends some time in kindergarten and in general frequently encounters infections, the risk of development of autoimmune

diseases at an older age decreases [6, 7]. The study by Lopez-Serrano with co-authors [8] indicates an increased risk of IBD for people with higher education and high social level that also emphasizes the potential role of the «hygiene hypothesis» in their occurrence.

Part of the «old friends hypothesis» is the proposition that infestations have a significant impact on the formation of the immune system, and the last decades are characterized by a decrease in incidents of helminthiasis in economically developed countries. Immunomodulatory properties of helminths' metabolism products are studied in the treatment of autoimmune diseases, including IBD, multiple sclerosis, rheumatoid arthritis and type 1 diabetes [9]. In 2005 [10, 11] the effective influence of helminths on the treatment of IBD resistant to traditional pharmacological therapy was demonstrated. But subsequent follow-up has not confirmed the positive impact of helminthotherapy. Other studies prove that the interaction of helminths with the human body is not a symbiosis, as is the case with gut microbiota. Helminthiasis requires treatment [12], as they have adverse clinical consequences.

Finally, the hypothesis of «biome depletion» explains the increase in the incidence of IBD in terms of loss of species diversity and changes in the composition of the commensal microbiome in the human body [13]. Changes in microbiota diversity occur as a result of breastfeeding refusal in infancy, the use of antibacterial drugs, genetic predisposition. But the greatest impact on intestinal microbial community is due to dietary preferences («westernization») and changes in basic approaches to nutrition (widespread use of semi-finished products, sweeteners, preservatives, taste modifiers, etc.), various technologies for cooking and preserving food, modern methods of water purification. All these factors make a significant contribution to the increase in the prevalence of autoimmune pathology, according to a number of researchers [14-16].

Study Objective

To assess the significance of surrogate markers of the «hygiene hypothesis», the «old friends theory» and the hypothesis of «biome depletion» in the development of UC among the population of the Western Siberia region.

Materials and Methods

Retrospective case-control study was conducted during the period from 2016 to 2018. The initial data was collected in the form of an active questionnaire (interview). The study included all patients with UC hospitalized in the Department of Gastroenterology of the Regional clinical hospital of Omsk region for the specified period. The diagnosis of UC was established on the basis of clinical manifestations, characteristic endoscopic and histological changes of the colon, according to the clinical recommendations of the Russian Gastroenterological Association and the Association of Coloproctologists of Russia for the diagnosis and treatment of UC. The comparison was made with a control group consisting of healthy environment of researchers comparable in age ($U = 13.38$; $p = 0.1760$) and sex ($2I = 2.72$; $p > 0.05$) with a group of patients with UC. All respondents gave voluntary informed consent and were included in the study.

The main group consisted of 81 patients (men — 42, women — 39) diagnosed with UC at the age of 18–79 years. The median age of patients at the time of the survey was 48 (32–60) years. The median age at the time of UC debut in all patients was 40 (28–54) years, in men — 40.5 years, in women — 32 years. The median time from the first symptoms of UC to diagnosis was 6 (1–12) months.

The control group consisted of 39 healthy respondents (men — 14, women — 25) aged 22 to 81 years. The median age of respondents was 46.0 (26.0–52.0) years. For men it was 36.0 ± 7.7 %, and for women — 64.0 ± 7.7 %.

We explored the major surrogate markers of the «hygiene theory», the «old friends hypothesis» and the «biome depletion» hypothesis: past infestations, pets in childhood, use of antibiotics, breastfeeding, family size (number of siblings), attendance at preschool institutions, accommodation in a dormitory while studying, accommodation in a city or village, type of drinking water supply and the type of water respondents use for drinking. Under the theory of «biome depletion», in addition to the above markers, a study of sugar consumption rate was carried out. Simple carbohydrate intake was calculated based on the number of cups of tea and/or coffee per week and the number of teaspoons or cubes of sugar that the interviewee puts in one cup. It was

decided not to include in the study questions on education and social status, because they, in our opinion, are not indicators of a better hygienic condition.

Methods of descriptive statistics were used to systematize and describe the data. The median and interquartile range were used to describe the groups by quantitative characteristics. The frequency of qualitative features is given as a percentage, taking into account the standard error of the indicator. The Mann-Whitney U-test was applied to compare groups by quantitative characteristics. To compare the groups by qualitative characteristics, we used the calculation of 2I-statistics (Kullbak information statistics), considered as a variant of nonparametric analysis of variance. The results were considered significant at $p < 0.05$. Statistical software package Statistica 6.1 was used for statistical data analysis.

Results and Discussion

According to the results of the study there were no statistically significant differences between patients with UC and healthy respondents in the presence of infestations in history, pets in childhood, taking antibacterial drugs, breastfeeding in childhood, place of residence, type of drinking water supply, allergies to food. Table 1 presents the results of the interview.

Families of parents in two groups of respondents were small ($M=2.0$ children). The main group had 48.1 ± 5.6 % of large families (3–7 children), and the control group — 43.6 ± 7.9 % of large families. There are no statistically significant differences between the groups ($2I = 1.77$; $p > 0.05$).

The analysis and comparison of frequency of visits to preschool institutions and accommodation in a dormitory for all respondents were carried out. It was found that kindergartens more often visited by healthy respondents 61.5 ± 7.8 % in comparison with patients with UC — 40.7 ± 5.5 % ($2I = 4.59$, $p < 0.05$), and that fact was statistically significant. But there are no statistically significant differences between groups that lived in a dormitory at school (44.4 ± 5.5 % of patients with UC and 33.3 ± 7.5 % of the control group). The distribution of participants in the study on attendance of preschool institutions and accommodation in a dormitory at school is shown in Figure 1.

Table 1. The results of the survey of ulcerative colitis patients on the main indirect markers of the «hygiene hypothesis»

Questions, answer codes	Code 1 frequency in the main group, %	m	Code 1 frequency in the control group, %	m	2I-statistics	p
History of infestations (1 — yes, 2 — no, 3 — I do not know)	25.9	4.9	21.1	6.6	0.98	>0.05
Pets in childhood (1 — yes, 2 — no)	92.6	2.9	92.3	4.3	0.00	>0.05
Antibacterial drugs (1 — yes, 2 — no, 3 — I do not know)	25.9	4.9	30.8	7.4	0.96	>0.05
Breastfeeding in childhood (1 — yes, 2 — no, 3 — I do not know)	82.7	4.2	89.7	4.9	3.06	>0.05
Place of residence (1 — city, 2 — village)	39.5	5.4	43.6	7.9	0.18	>0.05
Type of drinking water supply (1 — centralized, 2 — non-centralized, 3 — centralized and non-centralized, 4 — imported water)	77.8	4.6	92.3	4.3	5.9	>0.05
Food allergies (1 — yes, 2 — no, 3 — I do not know)	13.6	3.8	15.8	5.9	1.44	>0.05

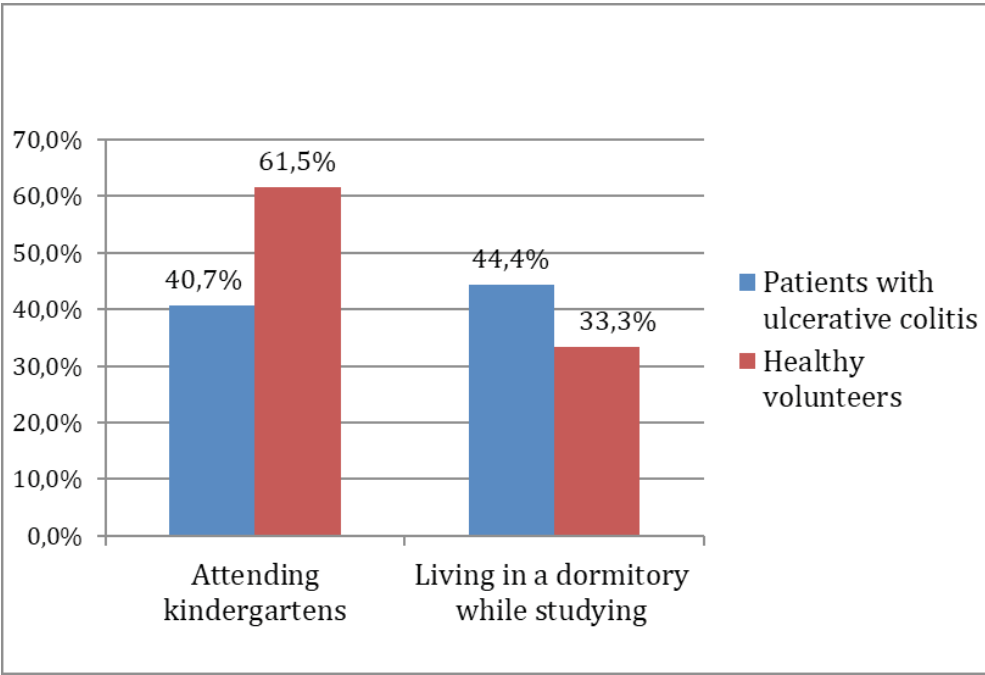


Figure 1. Attending kindergartens and living in a dormitory while studying

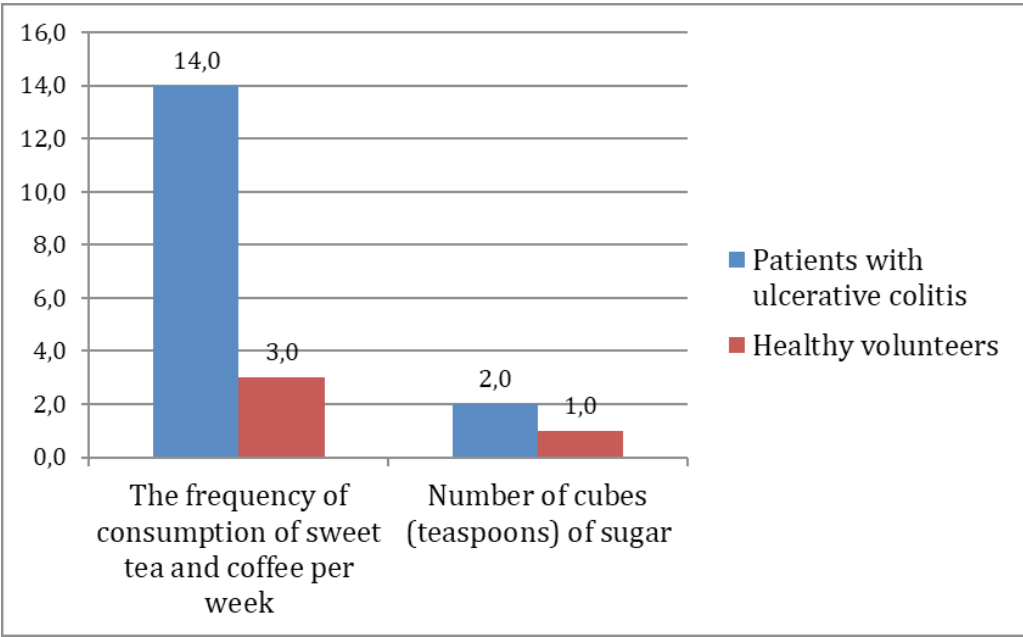


Figure 2. Sweet tea and coffee use

The «hygiene hypothesis» and the theory of «old friends» suggest that attending kindergartens has a beneficial effect on the harmonious development of the human immune system. Children’s bacterial infections and infestations, which have low pathogenicity, play an important role in the formation of immunity.

There are no statistically significant differences between groups by type of drinking water supply and type of drinking water used. We analyzed such parameters of the type of drinking water supply as centralized, non-centralized, or both centralized and non-centralized, or imported water. When answering the question «What kind of water do you use to drink?» respondents chose between the following options: boiled, not boiled, settled, bottled, filtered. The survey showed that 33.3 ± 5.2 % of respondents in the main group and 33.3 ± 7.5 % in the control group used boiled water for drinking. At the same time, 77.8 ± 4.6 % of patients with UC and 92.3 ± 4.3 % of healthy respondents use centralized water supply.

Features of consumption of sweet tea and coffee in the study groups are shown in Figure 2.

Patients with UC have a clear tendency to more frequent consumption of these drinks with sugar (median — 14.0 (1.0–21.0) times a week) compared

with healthy respondents (median — 3.0 (0.8– 14.0) times a week). However, there were no statistically significant differences between the groups in the frequency of consumption of tea and coffee with sugar during the week ($p = 0.06$). In addition, we found that patients with UC put statistically significant ($p = 0.04$) more cubes (teaspoons) of sugar in one cup of tea and/or coffee (2.0 (1.0–3.0) teaspoons; 1.0 (1.0–2.0) teaspoons, respectively). According to the «biome depletion» theory, the gut microbiota undergoes certain specific changes that occur not least under the influence of excessive consumption of food rich in simple carbohydrates.

Conclusions

Of the studied indirect markers of the «hygiene hypothesis» and the theory of «old friends», only one — attendance at preschool institutions ($2I = 4.59$) — affects the risk of UC in the population of Omsk region, $p < 0.05$.

In the hypothesis of «biome depletion» significant differences were found in the consumption of simple carbohydrates: patients with UC consumed, in the period before the onset of the disease, more sugar with tea and/or coffee compared with healthy respondents ($U = 1214.0$; $Z=2.0$; $p=0.04$).

Our study demonstrated the contribution of such factors to the emergence of UC as rare attendance of preschool institutions and the consumption of a large amount of monosaccharides in patients with UC in the period before the onset of the first symptoms of the disease compared with healthy respondents.

Conflict of interests

The authors declare no conflict of interests.

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