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Clinical and epidemiological aspects of ulcerative colitis in the Irkutsk region

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ABSTRACT AIM: to study sociodemographic, clinical and epidemiological features in patients with ulcerative colitis in the Irkutsk region (Russia).

PATIENTS AND METHODS: the database of the Irkutsk IBD Center included 1,122 patients with ulcerative colitis (UC) registered from 01.01.2006 to 31.12.2019. The study is retrospective with a focus on the results of follow-up, check up and treatment in different periods of their disease (acute attack, chronic course, remission). Statistical analysis was performed according to the principles of the International Committee of Medical Journal Editors (ICMJE).

RESULTS: the incidence of inflammatory bowel disease in the Irkutsk Oblast over the previous 14 years has increased by 2.7 times, of ulcerative colitis — by 3.1 times and was 3.91 person-years per 100,000 population. The prevalence of UC was 68.5 per 100,000 population. The annual increase in new UC cases was 46.6 ± 8.2 . Most patients had total lesion (68.4%) and moderate-to-severe disease (46.9%). Extra-intestinal manifestations (13.6%) were represented by skin lesions (40.7%). Body weight deficiency occurred in 9.9% in females and in 5.1% in males. The probability of colectomy was 1.4/100 patient-years (follow-up period was 7049.5 patient-years; n = 1122). Patients underwent urgent operations in 76.3%. Postoperative mortality was 1.03/100 patient-years (exposition time — 291.6 years, n = 3). Total mortality for the entire follow-up period was 1.8% — 0.34/100 patient-years (exposition time — 4440.8 years).

CONCLUSION: objective epidemiological data, clinical features and treatment options for patients with ulcerative colitis in long-term follow-up in the Irkutsk Oblast are presented. The results of such studies on a national scale can serve as a platform for further scientific research and planning of socio-economic programs.

KEYWORDS: ulcerative colitis, incidence, prevalence, non-surgical treatment, surgical treatment

CONFLICT OF INTEREST: the authors declare no conflict of interest

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INTRODUCTION

Ulcerative colitis (UC) refers to chronic inflammatory bowel diseases of unclear etiology, with lesions of the large intestine and suspected multifactorial trigger components with inadequate immune response in genetically predisposed individuals [1]. The annual incidence of UC varies and is observed in the range of 8.8–23.1 per 100,000 patient-years in North America; 0.6–44.0 in Europe and 7.3–17.4 in Oceania [2]. In the XXI century, the incidence of UC in developed Western countries has stabilized. At the same time, since the nineties of the XX century, according to an annual analysis, there has been an increase in the incidence in Asia, Africa, South America and Brazil by 14.9% [10.4–19.6], in Taiwan — by 4.8% [1.8–8.0]) [1,2]. In China, in the year of 2000, the diagnosis of UC was detected in 10,000 patients, and in 2010, the diagnosis of inflammatory bowel diseases (IBD) was already recorded in 266,394 [3]. In general, the first peak of morbidity occurs in the age group of 20-40 years, and the second — after 60 years, with the same gender distribution [2]. It is noted that in developing countries, UC is a more common disease than Crohn's disease (CD). In India, the incidence of UC is 6.02 per 100,000 population, which is much lower than in the USA (8.8 per 100,000) and Sweden (20.0 per 100,000). Numerous studies have shown the predominance of the urban population among patients with UC [4,5]. Attention is drawn to the existing worldwide spread of data on morbidity (0.4-44.5 per 100,000 population) and the prevalence of UC (from 1.5 to 505.0 per 100,000 population) within and between geographical regions, reaching maximum values in the countries of Scandinavia, North America, Canada, Israel. The prevalence of IBD is expected to continue to increase in high-income countries, and is also likely to accelerate in developing countries. This is partly due to the growing number of cases of UC in old age and the aging of patients, as well as a decrease in mortality due to the introduction of genetically engineered biological therapy (GEBT) into practice and a change in the paradigm of both conservative and surgical treatment [6-8].

The indicators of mortality in UC are in a wide range of values and depend on the socio-economic level of the reporting country. According to a meta-analysis published in 2007 by Jess, T. et al., among patients with UC, the average percentage of deaths was 17% (11; 30). In this subgroup of patients, the most common causes of death were colorectal cancer (CRC) 37% (24; 44) and surgical or postoperative complications 44% (17; 100).

Other causes indicated by the authors were associated with a severe course of the disease (toxic megacolon, bowel perforation, mesenteric thrombosis, secondary myocardial infarction on the background of anemia and decompensated liver disease due to primary sclerosing cholangitis) [9].

The number of population-based studies of UC in Eastern Europe, including in the Russian Federation, is limited. The prevalence of UC in Russia consists of the results of individual epidemiological studies and data from the registers of individual healthcare institutions [10]. According to the Ministry of Health of Russia, the increase in UC from 2012 to 2015 was 31.7%. According to published data from the leading centers of IBD, the prevalence of UC in the Moscow region is 19.3 per 100,000 population; 40.0 in the Republic of Tatarstan; 49.0 — in the Novosibirsk region; 22.0 per 100,000 adult population in the Chelyabinsk region [11,12,13].

AIM

The purpose of this study is to evaluate the clinical and epidemiological indicators and sociodemographic characteristics of patients suffering from ulcerative colitis living in the Irkutsk region and Irkutsk city.

PATIENTS AND METHODS

The Irkutsk region is located in the southeastern part of the Siberian Federal District; the area of the territory is 774.8 thousand square kilometers. In the west, the region borders with the Krasnoyarsk Territory, in the northeast with the Republic of Sakha (Yakutia), in the east — with the Trans–Baikal Territory, in the east and south — with the Republic of Buryatia, in the southwest — with the Republic of Tyva. The population of the region as of 2021 was 2,375,640 people. 78.8% of the region's population lives in urban areas. The population density is low — 3.07 people/km².

In connection with the data of Irkutsk Scientific Center of Surgery and Traumatology (ISCST), on the basis of the Irkutsk Regional Clinical Hospital (IRCH), since 1996, all patients of the city and region with an verified or suspected diagnosis of inflammatory bowel disease were sent to the outpatient unit for coloproctologist's consultation. By the order of the chief physician of the IRCH dated 01.03.2006, the IBD office was established on a functional basis. By that time, a separate registry for patients with IBD had been created, internal documentation had been developed, and an electronic unified database of patients had been created. This allowed the authors to analyze the incidence, prevalence, and features of clinical manifestations of IBD in long-term follow-up. The present study is based on a prospective and retrospective analysis of the results of follow-up, tests and treatment of patients in different periods of the disease (acute, chronic, remission), with an established diagnosis of ulcerative colitis in accordance with the diagnostic criteria of the disease [14].

The unified database is constantly updated and includes personal data, information about the onset of the disease, severity of the course, extra-intestinal manifestations, concomitant pathology, medications received, surgical treatment and other indicators, a total of 126 parameters [15]. All the patients signed an informed consent to the use of depersonalized information for scientific purposes.

In the period from 01.01.2006 to 31.12.2019 in the database of the IBD center of Irkutsk city 1,122 patients suffering from UC were registered. The period of 2020–2021 was excluded from the epidemiological analysis due to the conversion of medical facilities to provide assistance to the population with the new COVID-19 coronavirus infection and restrictions in working with profile patients.

To calculate the epidemiological characteristics, the generally accepted indicators "prevalence" and "morbidity" per 100,000 inhabitants, the indicator "person-years"/"patient-years", which most accurately reflects the real picture of the phenomenon under study and directly includes in the denominator the time of observation of a specific object, were used [16].

Statistical processing of the results of the study was carried out using the Statistica for Windows 10.0 program (StatSoft Inc., USA). The statistical analysis was performed according to the principles of the International Committee of Medical Journal Editors (ICMJE). Quantitative data are described using averages with the error of the mean, minimum, maximum and median with upper and lower quartiles, rate and fractions were calculated (in %). Descriptive statistics methods were used to generalize and evaluate demographic continuous and discrete variables. To describe qualitative indicators, rate and fractions (in%), a two-way 95% coincidence interval (95% CI) were calculated.



Figure 1. Age of patients at diagnosis (years)

Statistical hypotheses were tested at a critical significance level of p < 0.05.

The study was approved by the local Ethics Committee of ISCST within the framework of research No. 01201280993 (0543-2018-0018) State Registration, 2018.

RESULTS

Socio-Demographic Characteristics of Patients

In the period from 01.01.2006 to 31.12.2019, 1,122 people suffering from UC were registered in the database, of whom 619 (55.2%) were females, 503 (44.8%) were males; the ratio of females to males was 1.2:1.0. The average age of patients at the time of registration in the database was 43.1 ± 0.5 years (min-18.0; max-91.0). The maximum number of patients n = 532 (47.4%) was observed in the age group from 21 to 40 years, patients from 40 to 60 years were 32.7% (n = 367). The average age of the disease onset (the time of onset of UC symptoms) was

recorded at 37.1 ± 0.5 years (min-3.0; max-87.0 years). The distribution of patients by age groups at the time of diagnosis of UC is shown in Figure 1 and falls on the young age from 20 to 30 years — 603 (54.4%) patients.

The median time from the appearance of the first symptoms to the diagnosis of UC was 6.5 months (0.3-12.4); on average, the diagnosis of UC was established after 1.2 ± 0.1 years. The minimum time from the onset of the disease to the diagnosis was 3 days, in single cases (the first super-severe or severe) acute attack of UC; the maximum time from the appearance of intestinal symptoms to the diagnosis of UC in our study was 38 years, when the patient was observed and treated throughout life with various diseases of the gastrointestinal tract. The median history of UC in the cohort of patients was 7.0 years (0.5–14.0). According to the survey, patients associated the onset of the disease and subsequent exacerbations with the following causes: psychological trauma, stress — 21.8%; viral infection — 18.2%; pregnancy — 16.4%; for no apparent reason — 14.5%; harmful



Figure 2. Incidence of inflammatory bowel disease and ulcerative colitis per 100,000 population in the Irkutsk region (01.01.2006–31.12.2019)

industries — 12.7%; climate change — 9.1%; intestinal infections in history — 7.3%

About a quarter of patients gave up smoking due to their illness, 63.7% never smoked on average and 7% of patients continued to smoke.

Disability due to the underlying disease was recorded in 24.2% (n = 269) of cases, and the overwhelming majority (85%) of patients were identified as group 3.

According to social status, patients were distributed as follows: most of them work — 61.5%, 22.6% do not work, pensioners — 11.8%, students — 4.0%, the share of military personnel is 0.1%. In the Irkutsk region, more than 38% of patients with ulcerative colitis live in the regional center, the incidence ratio "city/village" was 1.6:1.0.

Incidence and Prevalence of Ulcerative Colitis in Irkutsk city and Irkutsk region

Over a 14-year follow-up period, the average incidence rate corresponds to 2.75 ± 0.95 (min-1.55; max-4.83) per 100,000 population (Fig. 2) or 3.59 per 100,000 person-years. Every year we register 46.6 \pm 8.2 new cases of the disease in the IBD center.

The UC prevalence in the Irkutsk region is 46.9 per 100 thousand population, in the city of Irkutsk — 68.5 (Fig. 3).

Phenotypic, Clinical Manifestations and Course of Ulcerative Colitis

Burdened heredity for ulcerative colitis was traced in our cohort of patients in 3.0% of cases (n = 23).

At the time of inclusion of patients in the database, acute UC attack/exacerbation was detected in 22.7% of cases (n = 225), chronic recurrent course during remission in 48.3% (n = 795), continuous course of the disease — 29.0% (n = 325). The prevalence of patients with total large intestine lesion (E3) was revealed in 68.4% (n = 768); left-sided colitis (E2) was recorded in 19.7% (n = 221); proctitis (E1) — in 11.9% (n = 133). The course of the disease was dominated by patients with moderate-severe UC — 46.9% (n = 526), a third of patients were diagnosed with severe course — 30.5% (n = 342), in 22.6% of cases (n = 254) — mild.

Steroid resistance and steroid dependence were detected in 10.4% (n = 115) and 18.1% (n = 201), respectively.

Average Body Mass Index (BMI) in females was 24.95 ± 0.19 (min-15.4; max-46.8); in 9.9% of cases, the body mass index was less than 18.0. The average BMI in males was 24.91 ± 0.22 (min-15.6; max-40.0); in 5.1% of cases, the BMI was less than 18.0.



Figure 3. Prevalence of inflammatory bowel disease and ulcerative colitis per 100,000 population in the Irkutsk region

Extra-Intestinal Manifestations

Systemic extra-intestinal manifestations of IBD in patients with ulcerative colitis were detected in 13.6% (n = 152) of cases, which amounted to 2.1/100 patient-years (follow-up period 7,049.5 p/y, n = 1,122). In 77.6% (n = 118) there was an isolated lesion of one organ (skin, musculoskeletal system, eyes, oral mucosal layer and others), and in 22.4% of cases (n = 34) there was a combined lesion of 2 or more organs and systems.

In 40.7% of cases, skin lesions were noted (dermatitis, erythema nodosum, gangrenous pyoderma); arthropathies/arthritis were observed in 38.2% of cases; oral cavity lesions (aphthous stomatitis, glossitis) in 4.6%; the proportion of primary sclerosing cholangitis was 11.5%; eye lesions (uveitis, iridocyclitis, conjunctivitis, blepharitis) were observed in 5.3% of cases. Over 14 years of follow-up, 5 cases of colorectal cancer were detected, which amounted to 0.44% in the observed cohort of patients.

In 11.4% of cases (n = 127), patients with ulcerative colitis were diagnosed with other immune-mediated diseases: vasculitis, psoriasis, systemic scleroderma, myositis, autoimmune thyroiditis, rheumatoid arthritis, systemic lupus erythematosus, bronchial asthma, demyelinating diseases of the nervous system. Porphyria was observed in two patients. In 3.6% of cases (n = 40), oncological diseases of extra-intestinal localization were observed in the studied cohort of patients: cancer of the root of the tongue, uterus, ovaries, pancreas, lungs, bladder, retroperitoneal sarcoma, lymphoma, melanoma.

Conservative Therapy

The total cumulative exposure of drug treatment was 90.6% for 5-ASA drugs; 48.7% for systemic corticosteroids; 33.8% for immunosuppressants (azathioprine) and 10.0% for biological therapy during the follow-up period.

Treatment with azathioprine was received in the observed period by 374 patients (33.3%), in the course of observation, the drug was canceled for various reasons in 95 patients (8.5%). Biological therapy was received by 109 (9.71%) patients with ulcerative colitis, which amounted to 1.8/100 patient-years (follow-up period 7049.5 p/y, n = 1,122), in 27.9% of cases, GEBT

(infliximab) was prescribed as a "rescue therapy". The reasons for the cancellation of drugs of the tumor necrosis factor alpha (TNFa) blocker group were: loss of response in 21.2% of cases, adverse events — 21.2% (infusion reactions, urticaria, dermatitis, alopecia, opportunistic infections, including tuberculosis, lymphoma, leukemoid reaction); discontinuation of therapy at the request of the patient occurred in 10.5%; in two cases (1.9%), the ineffectiveness of the initiated "rescue therapy" was found in supersevere forms of ulcerative colitis, patients were operated on.

Surgical Treatment

Total rate of colectomies by the end of the follow-up period (within 14 years) was 8.7% (n = 97). The need for surgical treatment was 1.4/100 patient-years (follow-up period 7049.5 p/y, n = 1,122).

In 76.3% of cases, patients underwent emergency and urgent surgery (complicated severe and super-severe forms of ulcerative colitis), in 23.7% surgery was elective (inefficiency of all types of basic therapy, malignancy). Postop complications occurred in 10.6% of cases (n = 7). Postoperative mortality was 2.9% (n = 3) or, taking into account the time interval (exposure 291.6) 1.03/100 patient-years. All deceased patients were delivered from the districts in a serious condition with colon necrosis, peritonitis, multiple organ failure. In 2 cases, the cause of death was infectious complications (subtotal bilateral pneumonia, sepsis, DIC) and in one case, the cause of death was massive PE, on the background of sepsis.

Mortality

According to the summary data of the Irkutsk city and Irkutsk region medical institutions, 20 patients with ulcerative colitis died within 14 years in the observed cohort of patients. The following causes of death were determined: in the early postoperative period — 3 patients (52, 58, 84 years old); in 7 cases, death from malignant tumors of extra-intestinal localization (retroperitoneal sarcoma, tongue cancer, ovarian cancer — 2 cases, Klatsken tumor, pancreatic head cancer, lung cancer) of patients aged

27, 28, 33, 50, 57, 66, 70 years old, respectively; two patients died of colorectal cancer (27 and 62 years old); in two cases — cardiovascular events (43 and 73 years old); 2 patients (23 and 27 years old) with primary sclerosing cholangitis; (one patient died on the third day after liver transplantation; the second — against the background of progressive liver failure); in 1 case, the death of a 29-year-old patient occurred from respiratory failure (post-tracheostomy stricture trachea). Thus, the total mortality for the entire follow-up period was 1.8%; when converted to the "patient-time" indicator, the observation exposure was 4,440.8 years, the total mortality was 0.34/100 patient-years.

DISCUSSION

The incidence of IBD in the Irkutsk region over the previous 14 years has increased 2.7 times, ulcerative colitis — 3.1 times and amounted to 3.91 "person-years" per 100,000 population. It should be noted that these figures are much lower than the world data, but are comparable with the incidence in the countries of Central, Southern and Eastern Europe (Romania - 2.4, Cyprus — 2.9, Croatia — 3.1, Belgium — 3.6, Moldova — 3.9, Portugal — 4.4 person-years per 100,000 population) [17]. The prevalence of IBD on a global scale increased from 79.5 to 84.3 per 100,000 population from 1990 to 2017, in the UK it is 449.6, in Europe the prevalence of IBD varies significantly; in particular in Eastern European countries it is registered at 104.5 per 100,000 [18]. In the Irkutsk region, the UC prevalence was 68.5 per 100,000 population, IBD — 93.2, which is slightly higher than the values given in the Russian Federation. The present study was dominated by patients with total large intestine lesion (68.4%), which is twice as much as the data obtained both in foreign studies and in the ESCApe2 study — 55% [10]. Moderate-severe course of UC occurred in 46.9% of cases. The patients, both males and females, were of normal weight, the body mass index averaged 24.9 (norm 18.50–24.99). Body weight deficiency (< 18) was detected twice as often in females (9.9%). The dominant extra-intestinal manifestations in the Irkutsk region were skin lesions (40.7%), which in 22.4% of cases were combined with rheumatological or other. The proportion of immunosuppressive therapy prescribing, including GEBT, exceeded the indicators for Russia, due to the predominance of medium-severe and severe forms. The socio-demographic characteristics obtained in the study are comparable to global trends. The need for surgical treatment tends to decrease. Based on the analysis of the database of the unified IBD center of the Irkutsk region, objective epidemiological characteristics, clinical course features and treatment options for patients with ulcerative colitis in a long-term study were obtained.

CONCLUSION

The epidemic of immune-mediated diseases predicted in the world, in particular IBD, high treatment costs with extensive use of biological agents and small molecules, dictates the need to search for both etiopathogenetic mechanisms and features of ethnic cohorts of patients with a specific geographical reference. Filling information niches in the Russian Federation is a platform for further scientific research, with the possibility of forecasting and planning socioeconomic programs.

AUTHORS CONTRIBUTION

Concept and design of the study: Elena Yu. Chashkova, Evgeny G. Grigoryev, Vladislav E. Pak Collection and processing of the material: Natalia S. Korotaeva, Elena Yu. Chashkova, Liudmila R. Shedoeva, Natalia V. Tungusova Statistical processing: Natalia S. Korotaeva Writing of the text: Elena Y. Chashkova, Natalia S. Korotaeva Editing: Vladislav E. Pak, Evgeny G. Grigoryev

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