



# Age-related and Gender Aspects of Inflammatory Bowel Diseases in the Republic of Dagestan

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**Aim:** Creation of a patient registry in the Republic of Dagestan to study various aspects of the course and outcomes of IBD, depending on the age and gender of patients.

**Materials and methods.** We have created a register of IBD patients in the Republic of Dagestan. It included 168 IBD patients aged 17 to 70 years, 69 males and 99 females, the average age of patients with IBD was  $38.1 \pm 2.5$  years with an average duration of illness of  $6.19 \pm 0.71$  years. The diagnosis of IBD was established on the basis of the characteristic clinical picture of the disease, objective status, results of laboratory, endoscopic, X-ray and morphological research in accordance with Russian Clinical Guidelines

**Results.** The prevalence of IBD in the Republic of Dagestan is 5.41 cases per 100,000 population. The progression of IBD is more often observed in women, aged 30 to 39 years, residents of rural areas. Anemia (mainly chronic iron deficiency) was registered in 66.1 %, more often in women, its maximum frequency was noted in patients aged 20–29 years (80 %). Disability due to IBD was registered in 55.4 % of patients.

**Conclusions.** The creation of a register of IBD patients in the Republic of Dagestan is aimed at monitoring the state of health, timely monitoring of the effectiveness of therapy and improving the quality of medical care.

**Keywords:** inflammatory bowel disease (IBD), patient register, the Republic of Dagestan, anemia

**Conflict of interests:** the authors declare that there is no conflict of interest.

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## Возрастные и гендерные аспекты воспалительных заболеваний кишечника в Республике Дагестан

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**Цель исследования:** создание в Республике Дагестан регистра пациентов для изучения различных аспектов течения и исходов ВЗК в зависимости от возраста и пола пациентов.

**Материалы и методы.** Нами создан регистр пациентов ВЗК в Республике Дагестан. В него вошли 168 пациентов ВЗК в возрасте от 17 до 70 лет, 69 лиц мужского и 99 – женского пола, средний возраст пациентов с ВЗК составил  $38,1 \pm 2,5$  года со средней продолжительностью болезни  $6,19 \pm 0,71$  года. Диагноз ВЗК устанавливали на основании характерной клинической картины заболевания, объективного статуса, результатов лабораторного, эндоскопического, рентгенологического и морфологического исследований в соответствии с российскими Клиническими рекомендациями.

**Результаты исследования.** Распространенность ВЗК в Республике Дагестан составляет 5,41 случая на 100 000 населения. Развитие ВЗК чаще отмечается у лиц женского пола, в возрасте от 30 до 39 лет, жителей сельской местности. Анемия (в основном хроническая железодефицитная) зарегистрирована в 66,1 %, чаще у женщин, ее максимальная частота отмечена у пациентов в возрасте 20–29 лет (80 %). Инвалидность по поводу ВЗК зарегистрирована у 55,4 % пациентов.

**Выводы.** Создание регистра пациентов ВЗК в Республике Дагестан направлено на мониторинг состояния здоровья, своевременный контроль эффективности терапии и повышение качества медицинской помощи.

**Ключевые слова:** воспалительные заболевания кишечника (ВЗК), регистр больных, Республика Дагестан, анемия

**Конфликт интересов:** авторы заявляют об отсутствии конфликта интересов.

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## Introduction

In recent years, inflammatory bowel diseases (IBD), which include Crohn's disease (CD) and ulcerative colitis (UC), have become increasingly important all over the world. IBD is defined as chronic recurrent diseases of the gastrointestinal tract of unclear etiology, in the case of CD characterized by transmural, segmental, granulomatous inflammation of the mucous membrane, in the case of UC — immune inflammation of the mucous membrane of the colon with the development of both local and systemic complications [1, 2]. The incidence of IBD is increasing, including in Eastern European countries [3, 4].

The prevalence of IBD varies in different countries, while reaching maximum values in industrially developed regions. In England, Canada, and the USA, the prevalence ranges from 40–150 people per 100,000 population, and the incidence is 4–6 people [4–8]. In the Russian Federation, the prevalence is 3.5–4.5 people per 100,000 population, and the incidence is 0.8, ones which is slightly lower than in Western European countries [1, 2].

The trend is that the incidence of IBD increases every year, and mainly among the young able-bodied population, and it leads to early disability. This is a basis of high social significance of IBD. The clinical manifestations of IBD is very variable, which often makes it difficult to timely diagnose and prescribe adequate therapy, and this inevitably negatively affects the prognosis of diseases. This trend makes it relevant to study the course of IBD depending on gender, age, duration of the disease, as well as to assess the presence of complications and disability in various regions of the Russian Federation.

**Purpose of the work.** Creation of a patient registry in the Republic of Dagestan to research various aspects of the course and outcomes of IBD, depending on the age and gender of patients.

## Materials and methods

168 patients with IBD were examined. The diagnosis of IBD was established on the basis of the characteristic symptoms and signs (with examination of the perianal region, finger examination of the rectum), the results of endoscopic (colonoscopy with ileoscopy, fibrogastroduodenoscopy), X-ray and morphological studies. When verifying the diagnosis, the greatest attention was paid to such symptoms as diarrhea, accompanied by a rise in body temperature to subfebrile values, abdominal pain, anemia, weight loss, increased ESR; the presence of internal and external fistulas or infiltrate in the abdominal cavity. Laboratory tests evaluated hemoglobin, leukocytes,

platelet, ESR, CRP, albumin, ALT, AST, GGTP, alkaline phosphatase, K, Ca, Mg, Fe levels. The co-program was examined, fecal culture was performed to exclude the presence of intestinal infection, and ELISA was used to determine toxins A and B of *C.difficile*. Critical importance for the diagnosis of IBD was attached to endoscopic examination with targeted biopsy and subsequent histological examination of the material.

We have studied the features of the course of IBD and such parameters as age, gender, age of onset of the disease, duration of the disease, the presence of anemia, complicated course of the disease, disability, trophological insufficiency. The treatment was analyzed, including the frequency of prescriptions and the effectiveness of glucocorticosteroids (GCS).

The main criterion for inclusion in the register of IBD patients was the presence of a confirmed IBD disease per 100,000 population. The diagnosis of IBD has always been based on the clinical and morphological picture of the disease. The exclusion criteria were the presence of acute intestinal infections (shigellosis, salmonellosis, yersiniosis, campylobacteriosis, tuberculosis, dysentery), the presence of helminths and other parasites.

Statistical data processing was carried out using the BioStat software package (version 5.9.8.5). Statistical analysis was carried out according to a multi-level program: analysis of distributions of features and their numerical characteristics; descriptive parameters of statistics are represented by the average value, standard error, in some cases median, evaluation of maximum and minimum values. Qualitative signs were described using absolute and relative (%) indicators. The reliability of the differences between the groups was determined by the Mann-Whitney method. The critical level of significance when testing statistical hypotheses was assumed to be 0.05.

## Research results and discussion

We have created a register of IBD patients in the Republic of Dagestan. It included 168 IBD patients aged 17 to 70 years, 69 male and 99 female, the average age of patients with IBD was  $38.1 \pm 2.5$  years with an average duration of illness of  $6.19 \pm 0.71$  years.

The population of Dagestan according to Rosstat for 2020 is 3 110 858 people. The prevalence of IBD in the Republic of Dagestan, according to our data, is 5.41 cases per 100,000 population.

By gender, patients with IBD in our registry are distributed as follows: men — 41.1 % ( $n = 69$ ), women — 58.9 % ( $n = 99$ ), i.e. there was a slight predominance of females in the ratio of 1.43:1.0. According to the literature data, both an equal ratio of the

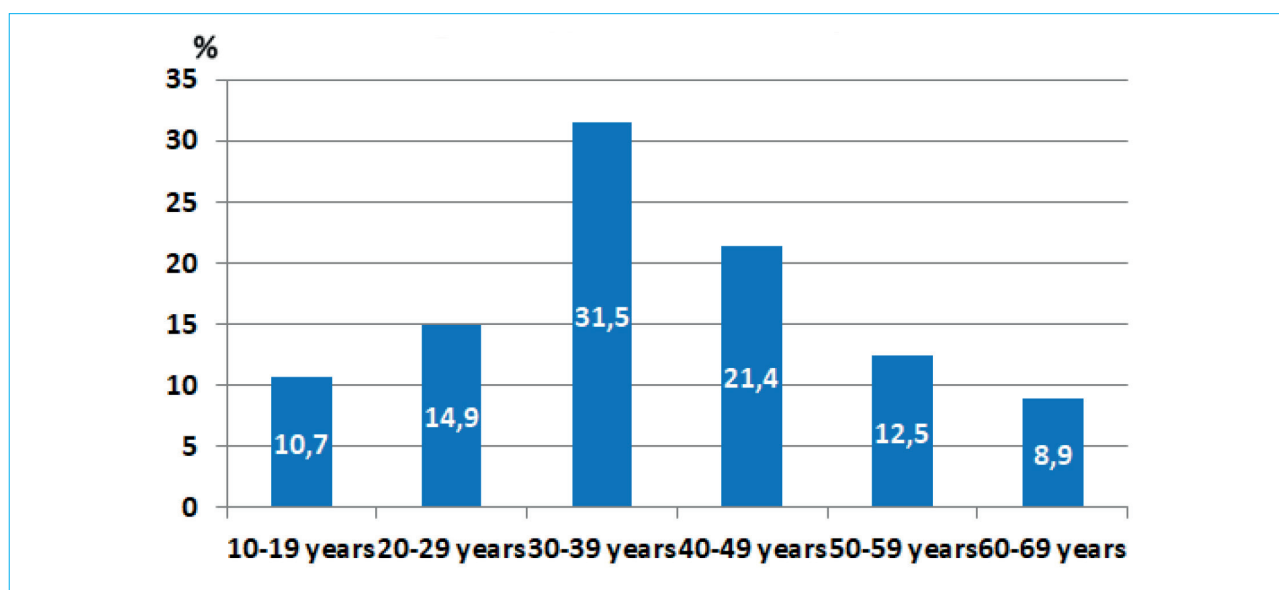


Fig. Distribution of IBD patients depending on age in the Republic of Dagestan

frequency of IBD cases among men and women [8] and a higher frequency of IBD in women [9] were noted. E.A. Belousova et al. (2018) analyzed the data of two epidemiological studies of the frequency, features of the course and treatment options of IBD in the Russian Federation (ESSAre and ESSAre-2): the ratio of women to men according to ESSAre was 1.1:1 in UC and 1.2:1 in CD (the differences were not statistically significant), according to ESSAre-2 in UC — 1.2:1 (53.5 % of women and 46.5 % of men), in CD — 1.25:1 (55.6 and 44.6 %) [10]. In general, the results on the frequency of IBD in men and women, both obtained by us and obtained in two studies of the Russian population of IBD patients, coincide with data from other countries.

We analyzed the age and gender characteristics of the course of IBD. When analyzing the register in the Republic of Dagestan by age categories with an interval of 10 years, the following features of the distribution of patients were revealed: the youngest male patient with a diagnosis of IBD was 17 years old, the oldest was 74 years old. The youngest female patient diagnosed with IBD is 16 years-old, the oldest is 70 years old. The largest number of IBD patients was in the age from 20 to 49 years (67.8 %), the smallest number — in the age range from 11 to 19 years (10.7 %) and from 60 to 69 years (8.9 %) (Fig.).

Gender analysis of the age structure of patients with IBD showed that the maximum number of males (55.0 %) are in the age range from 30 to 49 years, and the minimum number are aged 11 to 19 years (8.6 %) and aged 50 to 59 years (10.1 %). Among female patients, one in three was between the ages of 30 and 39. The minimum number of female IBD patients was aged from 60 to 69 years (6.1 %).

When assessing the ratio of women and men, it was revealed that in the age period from 11 to 19

years, there were 40 % more patients with IBD (ratio 1.40), and in the age period from 60 to 69 years, there was a predominance of males (frequency ratio — 2.13). In general, it can be noted that gender analysis of the distribution of IBD patients in the Republic of Dagestan by age categories revealed approximately the same trend of the maximum incidence of the disease at the age of 30 to 49 years in women and men, i.e. in the most able-bodied period, which determines the high social significance of this disease (table 1).

According to the Dagestan registry of patients with IBD, 63.1 % of IBD ( $n = 106$ ) patient lived in rural areas, and urban residents — 36.9 % ( $n = 62$ ). Consequently, the number of patients living in rural areas turned out to be 1.7 times more than patients from the urban population of the Republic of Dagestan. According to two epidemiological studies of the frequency, features of the course and treatment options of IBD in the Russian Federation, almost 80 % of IBD patients were urban residents, the ratio of urban and rural residents was 4:1 [10], which corresponds to the data of most epidemiological studies in other countries. Thus, the predominance of rural

Table 1. Distribution of IBD patients in the Republic of Dagestan by age and gender

Age (years)	Total $n = 168$		Men $n = 69$	Women $n = 99$
	$n$	%	%	%
11–19	18	10,7	8,6	12,1
20–29	25	14,9	13,0	16,2
30–39	53	31,5	27,5	34,3
40–49	36	21,4	27,5	17,2
50–59	21	12,5	10,1	14,1
60–69	15	8,9	13,0	6,1

Table 2. General characteristics of patients with IBD in the Republic of Dagestan

Indicators		N	Patients with IBD
Average age, years		$n = 168$	$38,1 \pm 2,5$
The average duration of the disease, years		$n = 168$	$6,19 \pm 0,71$
Gender	Male	$n = 69$	41,1 %
	Female	$n = 99$	58,9 %
Place of residence	City	$n = 62$	36,9 %
	Rural area	$n = 106$	63,1 %
Reception of GCS		$n = 106$	63,1 %
Anemia		$n = 111$	66,1 %
Disability		$n = 93$	55,4 %
Lower BMI		$n = 15$	8,9 %

residents among IBD patients identified by us in the Republic of Dagestan may represent a regional feature. Rural areas in the Republic of Dagestan are mainly represented by mountainous and foothill areas.

The general characteristics of IBD patients in the Republic of Dagestan are presented in Table 2.

Depending on age, the effectiveness of the inpatient treatment stage was evaluated to achieve clinical remission (improvement of well-being, decrease in stool frequency, disappearance of blood impurities in stool, decrease in temperature, leukocytosis, ESR) and the frequency of administration of glucocorticosteroids (GCS) (see Table 3). The greatest effectiveness of therapy during hospitalization (76 %,  $n = 19$ ) is observed in the age group from 20–29 years, and the lowest efficiency (46.7 %,  $n = 7$ ) in the age group of 60–69 years. In the other age categories, the effectiveness of therapy ranged from 57.1 % to 62.2 %.

GCS therapy was prescribed to 63.1 % of patients ( $n = 106$ ).

The indicators of the effectiveness of therapy in various age categories showed a certain parallelism with the frequency of the corticosteroids (methylprednisolone 24 mg/day or prednisolone 30 mg/day)

use. Only in the age group from 50–59 years, there was less effectiveness of IBD therapy with fairly frequent appointment of GCS (71.4 %).

The results obtained by us on the frequent appointment of GCS in the older age group are consistent with the analysis of the literature. An increase in the appointment of corticosteroids and a decrease in the appointment of biological drugs in elderly people with IBD compared with younger patients has been shown. Fears of the appointment of antibodies to TNF are probably due to the fear of an increase in infectious complications. At the same time, the appointment of GCS in the older age group may also be associated with a high frequency of adverse events, while the effectiveness has been little studied in clinical studies [11].

Disability due to IBD was registered in 55.4 % ( $n = 93$ ) of patients. Disability in patients with IBD is most often established at the age of 10–19 years (72.2 % of cases) and 50–59 years (66.7 % of cases). Less often, disability is established by IBD patients aged 60–69 years – in 26.7 % of cases.

According to the registry, anemia was often registered in patients with IBD, mainly chronic posthemorrhagic iron deficiency one: in 111 patients out of 168 (66.1 %). The maximum incidence of anemia

Table 3. Features of the course of IBD depending on age in the Republic of Dagestan

Age (years) $n = 168$	Effectiveness of inpatient treatment		Reception of GCS		Disability	
	$n = 103$	%	$n = 109$	%	$n = 93$	%
10–19 $n = 18$	11	61,1	12	66,7	13	72,2
20–29 $n = 25$	19	76,0	19	76,0	13	52,0
30–39 $n = 53$	33	62,2	35	66,0	31	58,5
40–49 $n = 36$	21	58,3	21	58,3	18	50,0
50–59 $n = 21$	12	57,1	15	71,4	14	66,7
60–69 $n = 15$	7	46,7	7	46,7	4	26,7



was observed in patients aged 20–29 years (80 %,  $n = 20$ ), as well as at the age of 11–19 years (77.8 %,  $n = 14$ ). The incidence of anemia decreases with the age of patients, and in the 60–69-year-old group it was registered in 26.7 % ( $n = 4$ ). This tendency to decrease the frequency of anemia in the elderly is probably associated with timely diagnosis and adequately selected therapy of anemia. Among males, anemia was detected in 34 out of 69 patients with IBD (49.3 %), and among females — in 68 out of 99 (68.7 %). Thus, anemia prevailed among females in a ratio of 1:1.39. The frequency of detected anemia did not depend on the place of residence of the IBD patient and was observed with approximately equal frequency in both urban residents (69.3 %) and rural residents (71.7 %). This indicates the same possibilities of diagnostic and therapeutic and preventive measures of urban and rural health care in this aspect.

According to systematic reviews, the frequency of anemia in CD ranges from 10.2 to 72.7 %, in UC does 8.8–66.6 % [12], and the overall frequency of anemia in IBD is 24 % [13]. Anemia is most often iron-deficient (in up to 57 % of cases) [13], which coincides with our data. Sufficiently high rates of anemia in the Republic of Dagestan with IBD should be interpreted from the point of view that anemia in the Republic of Dagestan in the absence of IBD is quite common and reaches 41.7 % in women and 26.6 % in men [14].

We have carried out the nature of the course of IBD depending on the duration of the disease (Table 4).

As follows from the data presented in Table 4, the occurrence of anemia is noted in 22 % of patients with IBD from the first year of the disease, with a longer duration of the disease, the prevalence of anemia increases and persists in the range from 65.3 % to 73.7 %.

There was no decrease in BMI in IBD patients during the first year of the course of the disease. The maximum frequency of patients with a decrease in BMI, which we consider as a manifestation of malnutrition, is observed with a duration of the disease from 2 to 5 years and reaches 13.9 %. With the

duration of the disease from 6 years and above, the frequency of patients with low BMI decreases to 7 %, and even to 6.7 %. At the same time, a decrease in BMI was more often registered in male IBD patients and was observed more than 2 times more often (20.9 %) than in female IBD patients (9.3 %) with a disease duration of 2 to 5 years.

GCS with a disease duration of up to 1 year was prescribed to 88.7 % of patients, which is explained by the need for induction of remission. With the duration of the disease from 2 to 5 years, as well as in the group of the duration of the disease from 6 to 10 years and more than 10 years, there was an approximate equal frequency of prescribing steroid drugs (55.6, 64.9 and 66.7 %, respectively).

The frequency of IBD patients with disabilities turned out to be the highest and reached 80 % with a disease duration of more than 10 years, and in the group with a disease duration of up to one year, there were none at all. In general, there is a direct correlation between the duration of IBD and the frequency of establishing a disability group.

Currently, there are separate examples of regional registers of IBD patients in the country, which allows us to apply a universal approach to organizing patient routing and providing a specialized environment for providing them with medical care. One such example is the IBD Diagnostic and treatment center established in St. Petersburg, which allowed organizing an individual program for the diagnosis and treatment of patients included in the regional registry. This contributed to the provision of timely centralized medical and diagnostic care, which as a result made it possible to reduce the time for verifying the diagnosis of IBD and reduce the proportion of patients with severe and moderate UC from 73.4 to 53.6 %, and CD — from 66.7 to 47 % per year [15]. Consequently, the strategy of creating regional registers of IBD and centers for the provision of high-tech medical care can contribute to a more efficient use of the resources of the healthcare system [16].

## Conclusion

The results obtained during the analysis of the created register of IBD patients allowed us to

**Table 4.** Characteristics of IBD depending on the duration of the disease

Disease duration	Anemia $n = 111$		Low BMI $n = 16$		Reception of GCS $n = 105$		Disability $n = 95$	
	$n$	%	$n$	%	$n$	%	$n$	%
Before 2 years $n = 9$	2	22,2	—	—	6	88,7	—	—
From 2 years to 5 years $n = 72$	47	65,3	10	13,9	40	55,6	34	47,2
From 6 years to 10 years $n = 57$	42	73,7	4	7	37	64,9	37	64,9
From 10 or more $n = 30$	20	66,7	2	6,7	22	66,7	24	80

understand that we are at the beginning of a difficult path of creating a register of IBD patients in the Republic of Dagestan and draw some conclusions:

1. The creation of a register of IBD patients in the Republic of Dagestan can help in monitoring their health status, timely monitoring of the effectiveness of therapy and in improving the quality of medical care.

2. The development of IBD in the Republic of Dagestan is more often observed in women, aged 30 to 39 years, residents of rural areas.

3. The most severe, complicated by anemia, course of IBD in the Republic of Dagestan was revealed in female individuals, which develops with the duration of the disease from 2 to 6 years, while malnourishment develops more often in males.

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