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INFLAMMATORY BOWEL DISEASES IN THE REPUBLIC OF MOLDOVA APPROACHED THROUGH THE *EUROPEAN CROHN'S AND COLITIS ORGANIZATION* - EPICOM-ECCO

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Summary

MALADIILE INFLAMATORII INTESTINALE ÎN REPUBLICA MOLDOVA PRIN PRISMA ORGANIZAȚIEI EUROPENE DE STUDIERE A BOLII CROHN ŞI A COLITEI ULCEROASE – EPICOM-ECCO

Cuvinte cheie: *colita ulceroasă, boala Crohn, incidență, prevalență.*

Introducere. *Incidența bolilor inflamatorii intestinale, boala Crohn şi colita ulceroasă, este supusă unor variații considerabile în întreaga lume, fluctuînd între 0 şi 24,3/100 000 de locuitori pentru boala Crohn, şi respectiv 0 şi 20,2/100 000 de locuitori, pentru colita ulceroasă, cu precădere în țările industrializate.*

Material şi metode: *În scopul aprecierii distribuției geografice a colitei ulceroase şi bolii Crohn în Europa, inclusiv Republica Moldova a fost elaborat protocolul unic – European Cooperative Study of Inflammatory Bowel Disease – EC IBD, de care s-au condus 20 de centre europene. În Republica Moldova au existat 2 centre, pentru populația pediatrică, IMSP Institutul Mamei şi Copilului, Departamentul de gastroenterology şi pentru populația adultă, Spitalul Clinic Republican, Clinica Gastroenterologie.*

Rezultate: *La nivel european, Republica Moldova se plasează cu o incidență de 2,9 la 100 mii populație, pentru populația pediatrică şi 4,3 la 100 mii populație, pentru populația adultă, ce o califică printre regiunile cu incidență mică din Europa de Est. În ambele loturi de pacienți, copii/adulți, incidența cea mai mare a fost în Europa de Vest 6,9 la 100 mii populație pediatrică şi respective 18,5 la 100 mii populație adultă, confirmînd încă o dată impactul factorilor de mediu în etiopatogenia bolilor inflamatorii intestinale.*

Concluzii: *Republica Moldova este o regiune cu incidență mică (2,9 - 4,3 la 100 mii populație) a maladiilor inflamatorii intestinale, deşi datele naționale remarcă un trend în ascensiune.*

Резюме

ВОСПАЛИТЕЛЬНЫЕ ЗАБОЛЕВАНИЯ КИШЕЧНИКА В РЕСПУБЛИКЕ МОЛДОВА В РАМКАХ ЕВРОПЕЙСКОЙ ОРГАНИЗАЦИИ ПО ИЗУЧЕНИЮ БОЛЕЗНИ КРОНА И ЯЗВЕННОГО КОЛИТА – EPICOM-ECCO

Ключевые слова: *язвенный колит, болезнь Крона, заболеваемость.*

Предпосылка/Справочная информация: *Заболеваемость воспалительных заболеваний кишечника, болезнь Крона и язвенный колит подлежит значительному изменению во всем мире, болезнь Крона приходится на долю населения от 0 и 24,3/100 000, и, соответственно язвенный колит на долю населения от 0 и 20,2/100 000, с уменьшением в промышленных зонах.*

Материалы и методы: *С целью определения географического распространения язвенного колита и болезни Крона в Европе, включительно в Республике Молдова, был разработан единый акт/протокол – Совместное европейский изучение воспалительного заболевания кишечника – EC IBD, которым руководствовалось 20 европейских центров. В Республике Молдова существовало 2 центра, для населения детей, ПМСУ Институт Матери и Ребенка, Отделение гастроэнтерологии и для взрослого населения, Республиканская Клиническая Больница, Клиника гастроэнтерологии.*

Результаты: *На европейском уровне Республика Молдова находится с уровнем заболеваемости от 2,9 на 100 тысяч населения, для населения детей, и для взрослого населения 4,3 на 100 тысяч населения, что определяет/квалифицирует с меньшей заболеваемостью в Восточной Европе. В обеих группах пациентов, детей / взрослых, заболеваемость была высокой в Западной Европе от 6,9 на 100000 детского населения, и, соответственно от 18,5 на 100 000 взрослого населения, еще раз подтвердив, влияние факторов окружающей среды в этиопатогенезе воспалительного заболевания кишечника.*

Выводы: *Республика Молдова является регионом с малой заболеваемостью (2,9-4,3 на 100 тысяч населения) воспалительных заболеваний кишечника, хотя национальные данные отмечают тенденцию роста.*

Introduction.

Inflammatory Bowel Diseases (IBD) are less widespread compared to other gastrointestinal diseases, but their medical and social impact is major, being determined by severe development associated with various complications, indefinite therapeutic approaches and tactics. In addition, over the past decades IBD, ulcerative colitis and Crohn's disease are characterized by a constant rise, with uneven geographical distribution [1, 2, 3, 5]. According to recent studies the geographical distribution of IBD has changed in the last 20 years. In most Western countries, the incidence of UC and CD has stabilized among the adult population, while in regions with a previously low incidence it has increased (Southern-Eastern Europe and Asia) [1, 2].

The incidence of inflammatory bowel disease, Crohn's disease and ulcerative colitis is subject to considerable variation worldwide, fluctuating between 0 and 24.3/100, 000 inhabitants for Crohn's disease, and 0 and 20.2/100, 000 inhabitants, for ulcerative colitis, particularly in industrialized countries. Although it is recognized that there are regions (Eastern Europe, Asia) where the level of IBD detection, and its recording is, respectively, below the level of detection in some Western European countries and in America. This does not explain the significant differences of IBD spread among these areas. Inhomogeneity of IBD spread on the world map suggests existence of certain features depending on the geographical area. Thus, maximal indices of UC prevalence were registered in the northern regions: Scandinavia, Canada and North America, with an annual increase of the disease in these areas from 8.3 to 24.5 cases per 100, 000 population. These epidemiological data allowed the experts to forecast for the coming decades an "epidemic" of IBD in Eastern Europe and Asia.

Extrapolation of incidence on the total European population records around 78 000 new cases of Crohn's disease and 178 000 cases of ulcerative colitis [1]. To assess the geographical distribution of UC and CD in Europe it was developed a unique protocol - *European Cooperative Study of Inflammatory Bowel Disease - EC IBD*, which has been followed by 20 European centers. Thus, since 2010 *European Crohn's and Colitis Organization* has initiated a new international multicenter prospective study, to which Eastern European countries joined, including the Republic of Moldova.

Purpose of study. To estimate epidemiological trends of inflammatory bowel diseases in the Republic of Moldova and to confirm the hypothesis of the west-east gradient in the distribution of ulcerative colitis and Crohn's disease in Europe by regcording all new cases of UC and CD in over 25 centers.

Material and methods

In order to assess the geographic distribution of ulcerative colitis and Crohn's disease in Europe, including the Republic of Moldova it has been developed a unique protocol - *European Cooperative Study of Inflammatory Bowel Disease – EC IBD*, which has been followed by 25 European centers. In the Republic of Moldova, there were two centers, PMSI Institute of Mother and Child, Department of Gastroenterology, for pediatric patients, run by Professor Ion Mihu; and Republican Clinical Hospital, Gastroenterology Clinic, for adult population, run by Țurcanu Svetlana, PhD. The inclusion of patients in the study was based on international criteria.

Copenhagen Diagnostic Criteria for CD (at least two of the criteria present):

1. History of abdominal pain, weight loss and/or diarrhoea for more than three months.
2. Characteristic endoscopic findings of ulceration (aphthous lesions, snail track ulceration) or cobble stoning *or* radiological features of stricture or cobble stoning.
3. Histopathology consistent with Crohn's disease (epitheloid granuloma of Langerhans type or transmural discontinuous focal or patchy inflammation).
4. Fistula and/or abscess in relation to affected bowel segments.

Copenhagen Diagnostic Criteria for UC (all three of the criteria present):

1. History of diarrhoea and/or rectal bleeding and pus for more than one week or repeated episodes.
2. Characteristic endoscopic findings of continuous ulceration, vulnerability or granulated mucosa.
3. Histopathology consistent with ulcerative colitis (neutrophils within epithelial structures, cryptitis, crypt distortion, crypt abscesses).

Results

The incidence and prevalence of inflammatory bowel disease in the Republic of Moldova were analyzed according to the National Center for Health Management of the Ministry of Health, but without nosologic specification during 2005-2014 [6]. Thus, both the incidence and prevalence of ulcerative colitis and Crohn's disease show a slow, but continuous increase, both among the pediatric population and adults.

Although national epidemiological data noted a slow increase in the incidence of inflammatory bowel diseases, at European level this rate ranks the Republic of Moldova (2.9 per 100, 000) among regions with a low incidence in Eastern Europe (Table 1), but in Western Europe it exceeds only Northern Italy (1.5 per 100, 000). However, Western Europe has the highest incidence (6.9 per 100, 000), followed by Central Europe (5.6 per 100, 000) and Eastern Europe at the bottom of the standings (4.7 per 100, 000).

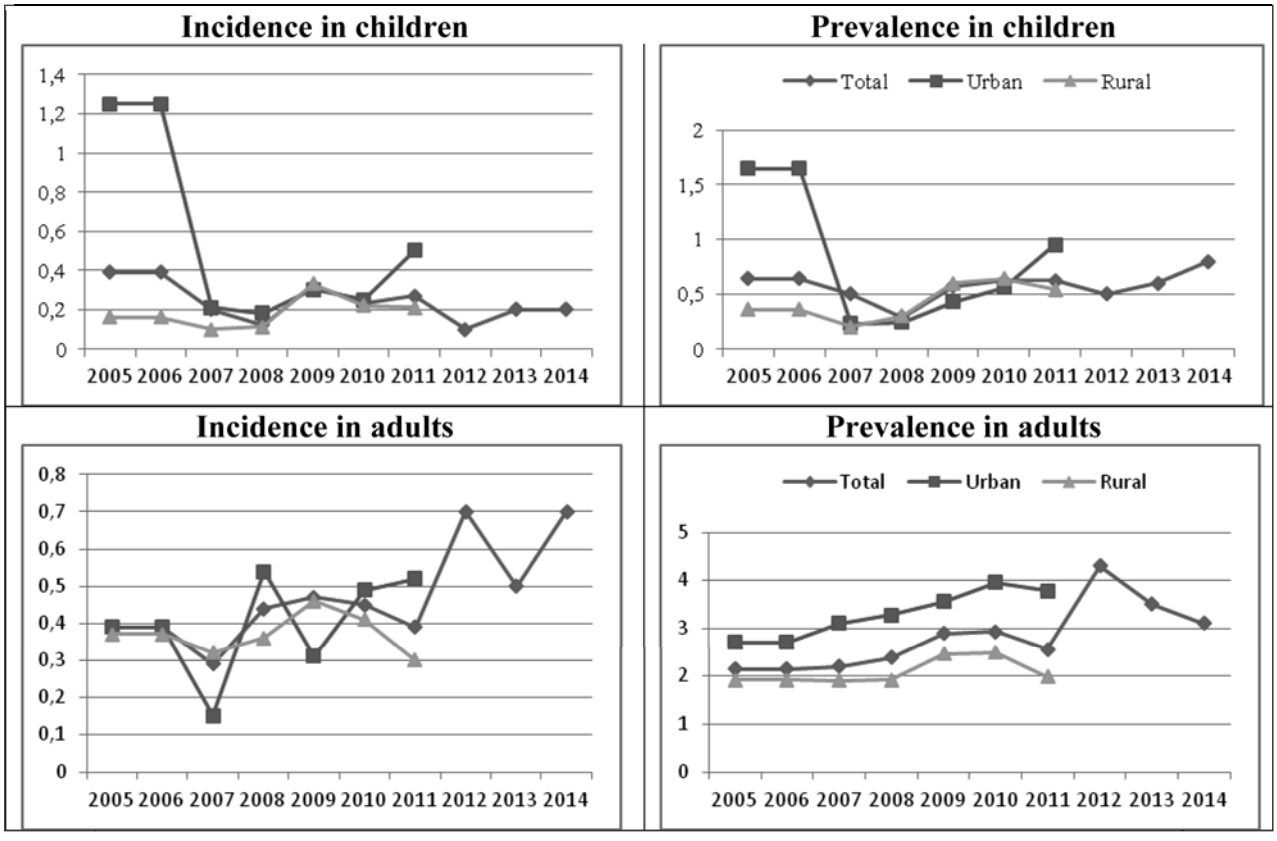

Figure 1. Incidence, prevalence in children and adults.

Table 1.

Crude incidence rates per 100,000 for inflammatory bowel disease, Crohn's disease, ulcerative colitis and inflammatory bowel disease unclassified in Europe for patients aged <15 years in 2010 [2]

	No. of patients	IBD	CD	UC	IC
Western European centres					
Denmark, Funen	6	7.1	4.7	2.4	0.0
Denmark, Herlev	4	8.1	2.0	2.0	4.0
Faroe Islands	1	9.4	0.0	9.4	0.0
Greece, Ioanninia	0	0.0	0.0	0.0	0.0
Italy, Northern Italy	4	1.5	0.4	1.1	0.0
Spain, Vigo	5	6.7	4.0	2.7	0.0
Eastern European centres					
Czech Republic, Prague	3	8.0	2.7	2.7	2.7
Estonia, Southern Estonia	3	5.6	5.6	0.0	0.0
Hungary, Veszprem	2	4.7	2.3	2.3	0.0
Lithuania, Kaunas	0	0.0	0.0	0.0	0.0
Moldova, Chisinau	17/**10***	2.9/**4,3***	0.2	2.7	0.0
All Western European centres, median	20	6.9	1.2	2.2	0.0
All Eastern European centres, median	25	4.7	2.3	2.3	0.0
All European centres, median	45	5.6	2.0	2.3	0.0

**for adult population*

Similar trends can be noticed among the adult population, Western Europe holds the standings, with an incidence of 18.5 per 100,000 population; among the countries with the highest incidence are Faroe Islands (81.5 per 100, 000 population), Sweden, Linköping (38.3 per 100,000 population), Denmark, Funen (30.7 per 100, 000 population), while the lowest incidence is in Greece, Ioannina (9.2 per 100,000 population). This spread argues that the frequency and the evolution of disease are

influenced by socio-economic level. The peak incidence was registered in countries with a high level of economic development, an advanced medical and hygienic level.

Epidemiological research carried out in Eastern Europe showed a lower prevalence of IBD 8.1 (7.2 - 9.2) per 100, 000 population compared with Western Europe. Thus, in Eastern Europe the region with the highest incidence is Hungary, Veszprem province (23.0 per 100, 000 population), followed by the Czech Republic, Prague (12.2 per 100, 000 population), while Romania and the Republic of Moldova have the lowest incidence with 4.3 and 4.1 per 100, 000 population, respectively. Although the incidence is low compared to Eastern Europe, recent epidemiological data show a steady increase of these diseases. Some explanations of increasing spread of IBD in these regions is "westernization" of lifestyle. This concept involves lifestyle changes, conditioned by advancing industrialization, the changing pace of life and diet (low consumption of natural products and increased consumption of refined and modified products, high proportion of easily assimilated carbohydrates and lipids in relation to insufficient consumption of plant fiber).

Central Europe was highlighted as an epidemiological center between Western and Eastern Europe, with an incidence of 15.2 (14.4-16.0) per 100, 000 population. The existence of the north-south gradient was not confirmed by this study because external impact factors investigated in this study (climatic conditions, smoking, economic level of life, peculiarities of nutrition, administration of contraceptives, etc.) were absolutely insufficient to explain this hypothesis confirmed by many prospective European multicenter researches, stating that the incidence of UC and CD proved to be 40% and 80% higher in the north centers compared to the south centers.

Conclusions

1. The incidence of Inflammatory Bowel Disease in the Republic of Moldova over the last 10 years has recorded a slow rising trend, both among the pediatric population and adults.
2. Eastern Europe, including the Republic of Moldova and Romania, are characterized by a lower incidence than Eastern and Central Europe, but with an increasing trend.
3. The increase in IBD spread in Eastern Europe is determined by "westernization" of lifestyle.
4. The north-south gradient was not confirmed by this study because external impact factors investigated in this study were absolutely insufficient to explain this hypothesis.

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