

## EPIDEMIOLOGY OF ULCERATIVE COLITIS IN NORTH- EASTERN ROMANIAN AREAS

Elena Toader<sup>1</sup>, Lidia Rusu<sup>2</sup>, Liliana Croitoru<sup>3</sup>, Oana Arhip<sup>4</sup>, Camelia Mihăilă<sup>5</sup>

1. Institute of Gastroenterology and Hepatology Iași, University of Medicine and Pharmacy, Iași, România
2. Institute of Public Health Iași, România
3. District Hospital Suceava, România
4. District Hospital Botoșani, România
5. District Hospital Bârlad, România

**Abstract.** The aim of the present study was to determine the incidence and clinical course of ulcerative colitis (UC) in North-Eastern (NE) Romania during 2000-2006. Ulcerative colitis represents a distinct entity of inflammatory bowel disease (IBD) with unknown etiology which affects young people. UC is ubicvitar disease with an incidence rate that varies greatly worldwide. **Material and method.** There were identified 301 UC cases with use of the diagnosis criteria for UC during the period of time from the year of 2000 till 2006. The incidence was estimated according to districts registered data recorded within – Health District Authorities. Clinical data concerning UC were registered according to medical (hospital) recordings. **Results.** UC incidence in NE Romania during 2000-2006 was  $1.75/10^5$  inhabitants recording a progressive increasing in the studied period. The distribution of the disease in all four districts was: Botoșani  $1.65/10^5$  inhabitants; Iași  $1.95/10^5$  inhabitants; Suceava  $1.83/10^5$  inhabitants and Vaslui  $1.57/10^5$  inhabitants. The incidence values were higher in urban areas than rural ones ( $2.23/10^5$  inhabitants vs  $1.21/10^5$  inhabitants). The mean age was 45.5 y with the distribution in age group and sex  $46.47 \pm 14.54$  y for male and  $44.48 \pm 15.37$  y for women, at the time of the diagnosis. Complications of the UC as proctitis were found in 35.3% of cases, left side colitis in 35.3% and pancolitis in 22.6% at the time of diagnosis. Severity of the first attacks evaluated according to Truelove and Witts criteria was mild in 41.7% cases, moderate in 38,2%cases, and severe in 20.1% cases. **Conclusion.** The low incidence of UC in NE Romania ( $1.75/10^5$  inhabitants) confirms the low frequency of the disease in this part of Europe. The progressive increasing of incidence UC during the period study and heterogeneity distribution in county as unknown, but the evidence support a possible role for behavioural factors (for example nutrition, life style). Socio-demographic characteristics, clinical features, disease extent and clinical course of UC are the same in low-as well as high-incidence area.

**Key words:** ulcerative colitis, incidence, clinical course

**Rezumat.** Rectocolita ulcerohemoragic (RCUH) reprezintă o entitate distinctă a Bolii Inflamatorii Intestinale cu etiologie necunoscută care afectează în special tinerii. RCUH este răspândită în întreaga lume dar cu variații mari de incidență de la o regiune geografică la alta. **Scopul** acestui studiu a fost evaluarea incidența și trăsăturile clinice ale RCUH în NE României în perioada 2000-2006. **Material și metodă.** În NE Românie în perioada 2000-2006, au fost identificate 301 de cazuri cu RCUH, diagnosticate prin utilizarea criteriilor diagnostice recunoscute. Datele necesare pentru evaluarea incidenței și trăsăturilor clinice

pentru fiecare caz de RCUH au fost preluate din înregistrările oficiale ale Autorității de Sănătate Publică, precum și din documentele medicale. **Rezultate.** În NE României în perioada 2000-2006 incidența RCUH a fost de  $1,75/10^5$  locuitori înregistrând o creștere progresivă în intervalul de studiu. Distribuția incidenței RCUH în cele 4 județe a fost: Botoșani  $1,65/10^5$  locuitori; Iași  $1,95/10^5$  locuitori; Suceava  $1,83/10^5$  locuitori și Vaslui  $1,57/10^5$  locuitori. Repartiția cazurilor pe medii de proveniență relevă o frecvență mai mare a RCUH în mediul urban ( $2,23/10^5$  locuitori) comparativ cu mediul rural ( $1,21/10^5$  locuitori). La momentul diagnosticului vârsta medie a fost de 45,5 ani cu următoarea distribuție în raport cu vârsta și sex:  $46,47 \pm 14,54$  ani la bărbați și  $44,48 \pm 15,37$  ani la femei. Evaluarea extensiei leziunilor la debutul bolii relevă proctită în 35,3% cazuri, colită stângă în 35,3% cazuri și pancolită în 22,6% cazuri. Severitatea puseului inaugural relevă 41,7% cazuri cu puseu ușor, 38,2% cazuri cu puseu moderat și 20,1% cazuri cu puseu sever. **Concluzii.** Incidența RCUH de  $1,75/10^5$  locuitori raportată pentru NE României în perioada 2000-2006 confirmă frecvența redusă a bolii în această regiune a Europei. Creșterea progresivă a incidenței RCUH în perioada de studiu și distribuția heterogenă în teritoriu sunt necunoscute, însă un posibil rol îl ocupă factorii comportamentali (nutriția, stilul de viață). Trăsăturile socio-demografice, aspectul clinic, extensia bolii și severitatea puseului inaugural sunt asemănătoare cu cele raportate și în zonele cu incidență RCUH crescută.

**Cuvinte cheie: rectocolita ulcerohemoragică, incidență, tablou clinic**

#### INTRODUCTION

Ulcerative colitis (UC) is closely related to another condition of inflammation of the intestines called Crohn's disease. Together, they are frequently referred to as inflammatory bowel disease (IBD). UC is ubicvitar disease with an incidence rate varies greatly worldwide between  $0,5-24,5/10^5$  inhabitants (1).

UC and Crohn's diseases are chronic conditions that can last years to decades. They affect approximately 500,000 to 2 million people In the United States. Men and women are affected equally. They most commonly begin during adolescence and early adulthood, but they also can begin during childhood and later in life.

It is found worldwide, but is most common in the United States, England, and northern Europe. It is especially common in people of Jewish descent. Ulcerative colitis is rarely seen in Eastern Europe, Asia,

and South America, and in the black population (2,3).

For unknown reasons, an increased frequency of this condition has been recently observed in developing nations.

Few dates are available on the epidemiology of UC related to incidence and prevalence in Romania. A recent study in South Eastern Europe, has reported an incidence of  $1/10^5$  inhabitants in Romania (the lower values within this part of Europe) (4).

Colon cancer is a recognized complication of chronic ulcerative colitis. The risk for cancer begins to rise significantly after eight to ten years of colitis. The risk of a patient with ulcerative colitis of developing colon cancer is also related to the location and the extent of their disease.

Serious complications are rare in these patients. In those with more extensive disease, blood loss from the inflamed intestines can lead to anemia, and may require treatment with iron supplements

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or even blood transfusions. Rarely, the colon can acutely dilate to a large size when the inflammation becomes very severe. This condition is called toxic megacolon. Patients with toxic megacolon are extremely ill presenting fever, abdominal pain and distention, dehydration, and malnutrition. Unless the patient improves rapidly with medication, surgery is usually necessary to prevent colon rupture.

Complications of ulcerative colitis can involve other parts of the body. Some patients (10%) can develop inflammation of the joints (arthritis). Some other patients have low back pain due to arthritis of the sacroiliac joints. Rarely, patients may develop painful, red, skin nodules (erythema nodosum). Yet others can have painful, red eyes (uveitis, episcleritis). These particular complications can lead to permanent vision impairment, eye pain or redness that requires the physician's evaluation. Diseases of the liver and bile ducts may also be associated with ulcerative colitis. For example, in a few patients with a condition called sclerosing cholangitis, the repeated infections and inflammation in the bile ducts can lead to recurrent fever, yellowing of skin (jaundice), cirrhosis, requiring the liver transplant.

**The aim** of the present study was to determine the incidence and clinical course of UC in North-Eastern Romania, during 2000-2006.

### MATERIAL AND METHODS

#### **Demographical data**

NE Romanian territory represents a mixed urban - rural county well

geographical delimited, which covers 24,327 km<sup>2</sup> (approximately 10.24% of Romania) with a population of 2,494,599 inhabitants (approximately 10.89% of Romanian population). The study area was divided between four districts (Iași 5470 km<sup>2</sup>, with 842,126 inhabitants and a population density of 153.95%, Suceava 8353 km<sup>2</sup>, with 719,134 inhabitants, and a population density of 86.09%, Vaslui 5318 km<sup>2</sup>, with 467,901 inhabitants, and a population density of 87.98%, Botoșani 4986 km<sup>2</sup>, with 465,438 inhabitants, and a population density of 93.35%). These data were collected from the Statistics Annuar of Romania (6).

#### **Population study**

The study population was demographically heterogenous, with a migration rate of 9.8% range and ethnically homogeneous. The access to well organized health care services was uniform.

The study included all the patients with the possible UC after wards endoscopical and histological confirmed by the Institute of Gastroenterology and Hepatology Iași, the only university medical specialized centre from the region, from the staff and technical support point of view.

The UC observation was performed by the family doctors in most of the cases followed-up by internal medicine, surgery and epidemiology physicians. Patients diagnosed in the same calendar year were included in the incidence calculation. The patients with acute or chronic infections disease, cancer, non IBD-disease or

insufficient information were not included in the study.

**Diagnoses criteria** (based on hospitalisation records, outpatients visits, endoscopic, radiological and histological evidence) were (7):

- typical case history with diarrhoea and/or blood/pus in the stool for more than a week or of repeated episodes;
- typical sigmoidoscopy with granulated, friable mucosa and ulceration of the surface mucosa.
- characteristic histologic and /or cytologic signs of inflammation, and
- radiological or colonoscopic sings, or both, or inflammation with a speculated, granulated inner surface of the colon proximal to the rectum and/or frank ulceration.

**Disease extent**

The extent of the disease has been described according to the endoscopical and barium enema change found at rectosigmoidian level for proctitis, extended to the splenic flexure for left side colitis or involving entire colon over them with concerned tendency bowel for pancolitis (8).

**Attacks of severity** were defined as mild, moderatly-severe and severe base on their symptoms, physical findings and laboratory values, according to the system described by Truelove and Witts.

**Date recording**

Socio-demographic and epidemiological parameters recorded in this study were included within a questionnaire who contained personal data, clinical

parameters, laboratory tests, endoscopic, hystologic and radiological results.

**Statistical analysis**

Data collections were performed by EXCEL program. Statistical analysis applied revealed an incidence comparable with other epidemiological study in South Eastern European Countries.

There were estimated the annual incidences, its distribution by age and sex, distribution of the different localizations of the UC according to age and sex and complications by age and sex.

**RESULTS**

A total of 301 patients were diagnosed as having UC during 2000-2006, of which 140 were women and 163 men. The median age of the diagnosis was 46.47 for men (ranged between 18 and 83 y) and 44.48 for women (ranged between 16 and 84 y). The mean annual incidence of UC in NE of Romania was  $1.75/10^5$  inhabitants (IC 95% 1.20 – 2.28). The rate of the annual incidence of UC increased progressively, ranging between  $1.60/10^5$  and  $1.96/10^5$  with a median number of 43 new UC cases/years. The annual incidence of the UC for each consecutives years, during the observed period (2000-2006) are showed in the figure 1.

The values of the incidence of UC in each county were  $1.93/10^5$  inh. Iași,  $1.83/10^5$  inh. Suceava,  $1.65/10^5$  inh. Botoșani and  $1.57/10^5$  inh. Vaslui.

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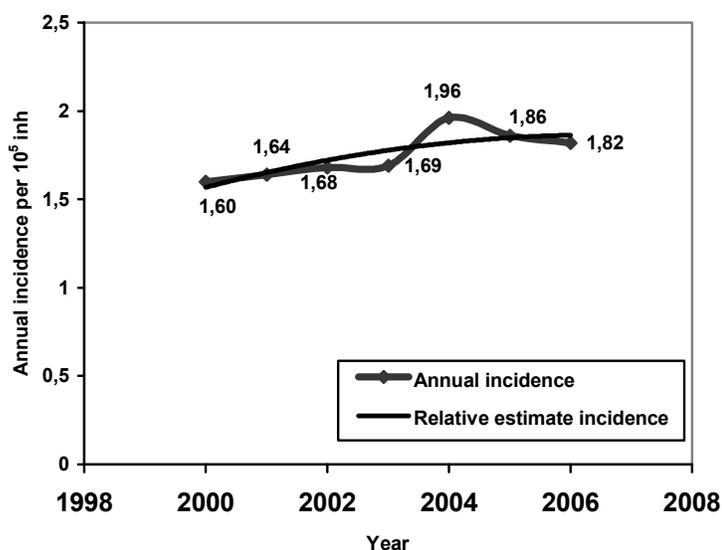


Fig. 1. Annual incidence rates and relative estimated incidence of UC

The mean annual incidence for UC in the urban area was  $2.32/10^5$  inhabitants and  $1.21/10^5$  inhabitants in the rural ones. The male-females ratio index was 1.1/1. The incidence rates were  $1.93/10^5$  in male and  $1.59/10^5$  in female. The mean annual incidence in different age groups was calculated for the period 2000-2006 as shown in figure 2.

The UC distribution by age interval reveals a bimodal pattern with progressive increasing incidence in men with a first peak established between 35-44 years and a second,

smaller peak of incidence in subjects with age over 65 years old.

Proctitis was found in 35.3% of cases, left side colitis in 35.3% and pancolitis in 22.6% at the time of diagnosis. In 24 cases (6.8%) the information about disease localization was incomplete.

The disease extent showed similarly distribution in all age groups except for young patients (< 30 y) in whom a significantly higher proportion of total colitis was found.

The proportion of patients with severe attacks of UC require 20.1%, moderate activity was noted in 38,2% cases and mild activity in 41,7%.

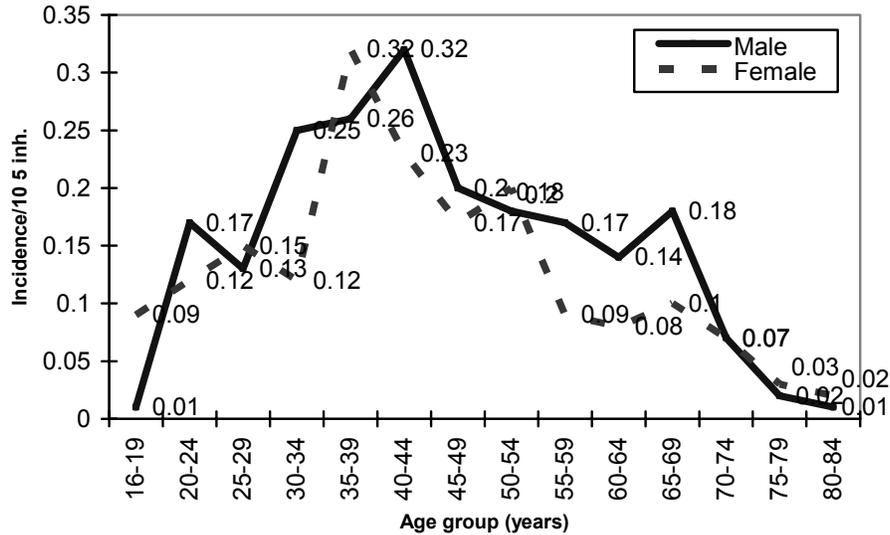


Fig. 2. Incidence of UC distribution by age and sex

#### DISCUSSION

The annual UC incidence rates registered values from  $1.60/10^5$  in 2000 to  $1.82/10^5$  in 2006, with an average rate of  $1.75/10^5$ . This is one of the lower values that have been reported of some studies in the field within SE Europe. The low values of UC registered in Romania, could be explained by the lower capacity of diagnosis.

A recent study aimed to evaluate UC incidence and prevalence rates in SE Europe reports an ascendant trend for countries as Hungary ( $5.9/10^5$ , range 1.6-11) and Croatia ( $3.9-5.9/10^5$ ), being comparable with the countries from North and West of Europe (9,10). Also, in other countries as Czech Republic ( $1.4/10^5$ ; 3.1), Poland

(1.8), Slovakia, Baltic countries (1.5; 1.7) there have been required lower UC incidence rates similarly with the values reported in our study (11, 12, 13). Low UC incidence rate in NE Romania ( $1.08/10^5$ ) was also reported in a multicentre national study which was performed in Romania over the period of one year (2002-2003) (5).

The heterogen distribution of the UC in area and finding of regional differences can suppose to exist of a gradient NE –  $0.76/10^5$ ; SE –  $1.32/10^5$ ; NV –  $1.13/10^5$ . Further studies are necessary in that sense. The progressive increasing of the mean annual UC incidence during the study period could be explained by the use up-to date diagnosis procedures.

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Environmental and life style changes could also have a role in the increasing values of the disease.

The distribution of the UC incidence cases in NE of Romania, although heterogenic, does not account significant differences between the 4 districts, except Iasi which has the highest incidence rate of the disease. The quality of the disease registration is very important for a good real estimation of the disease.

As an example, a few patients were susceptible to be recorded outside the county, representing a limit of an under estimation of incidence.

The urban/rural distribution of the disease by resident areas with differences in incidence represents a characteristic of UC previously documented. In our study the distribution of UC was less frequently in rural communities. There are consonant data with the literature that revealed the possible impact of the environmental factors on disease (14).

Most studies reported higher values of median age of the appearance of the disease. The incidence by different age group and sex reveals a bimodal pattern. The first peak was observed in 35-39 age groups for women followed by continuous decrease. The incidence first peak for men was noticed in 40-44 age groups followed by a second smaller peak at 65-69 age group.

The report extent of UC at time of diagnosis varied considerably with a frequency of 22% to 55% for proctitis and 19-30% for extensive colitis. This range includes our findings in the extent of the disease. The proportion of 35.3% proctites among incidence

cases of UC in our study is considered to be a good marker of the complete of the UC collection. There were the same aspects in the use of colonoscopy or radiology in 46% of all cases as complementary methods for diagnosis of UC extent with recent study in literature (15).

The severity of the first attack did not differ from the previously data in literature. An increase number of new patients were recorded during the study period as having initial mild activity at diagnosis. However, the frequency of the severity attack remained relatively stable.

### CONCLUSIONS

- This epidemiological study was performed in North-East part of Romania. It revealed a low incidence of UC, as comparable in the South-Eastern European countries.
- The progressive increasing of incidence UC during the period study and heterogeneity distribution in county are determined by unknown factors, but the evidence supports a possible favourizing role of behavioural factors (nutrition, life style).
- Socio-demographic characteristics, clinical features, disease extent and clinical course of UC are almost the same in low-as well as high-incidence areas.
- Further specific studies are needed in order to determine those factors responsible for a lower incidence in North-East part of Romania.

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