

# CLINICAL FEATURES IN CROHN'S DISEASE - A RETROSPECTIV BICENTRIC STUDY (BUCHAREST, TIMISOARA) DURING 2005-2009

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**Keywords:**  
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**Abstract:** The aim of our study is the characterization of Crohn's disease (CD) in terms of clinical onset, the degree of activity, the appearance and the topographical distribution of the lesions and the clinical and the pathological behavior of the disease. **Materials and Methods** The study group consists of adults (> 18 years) with newly diagnosed CD investigated in The Fundeni Institute, The Center of Gastroenterology and Hepatology and in the Department of Gastroenterology and Hepatology, of The Emergency County Hospital Timisoara during the period 2005-2009. **Results** The major signs and symptoms at admission were: chronic diarrhea in 59.4% of the cases, abdominal pain in 45%, weight loss (below 10% of the ideal weight) in 39.4% of the cases. By correspondingly Harvey-Bradshaw index, 27.2% of the cases were classified as having mild activity, 43.3% of the cases as moderate activity, 3.9% engaged in severe activity; 25.6% of the patients were classified as inactive clinically and biologically. Typical findings on endoscopy were: ulcers in 70.6% of the all cases, strictures in 14.5%, cobblestone pattern 18.3%, "skip lesions" in 11.1%, non-perineal fistulas in 1% of cases. By Montreal phenotype classification, patients are grouped in relatively equal proportions from 17 to 40 years and over 40 years; 56.6% of the cases were colonic disease, 32.2% ileocolonic disease and 11.2% small bowel disease; 72.2% of the cases were non-penetrating/non-stricturing, 14.5% stricturing, and penetrating 13.3%; perineal disease was present in 10% of the cases (56% fistulas and 44% abscesses). **Conclusions:** Although symptoms and signs at onset and endoscopic lesions are similar to those described in literature, the Montreal phenotype classification results confirm the previous studies that attest in Romania a late onset, a predominance of colonic disease and of non-penetrating/non-stricturing behavior and a reduced incidence of perianal disease. Most cases are moderately active CD, followed in relatively equal proportions by cases with mildly active and inactive CD. Percentage of severely active CD was very low compared with literature data. These data confirm the existence of a particular phenotype of CD in Romania.

**Cuvinte cheie:** boli inflamatorii intestinale, boala Crohn, clasificarea Montreal

**Rezumat:** Scopul studiului nostru constă în caracterizarea cazurilor de boală Crohn (BC) din punct de vedere al debutului clinic, al gradului de activitate, al aspectului și distribuției topografice a leziunilor și al comportamentului clinico-patologic al bolii. **Material și metodă** Lotul de studiu este alcătuit din pacienții adulți (>18 ani) cu BC nou diagnosticată investigați în Institutul Clinic de Gastroenterologie și Hepatologie Fundeni și în Clinica de Gastroenterologie și Hepatologie Timișoara, în intervalul de timp 2005-2009. **Rezultate** Principalele semne și simptome la internare au fost: diareea cronică în 59,4% din cazuri, durerea abdominală în 45%, scăderea ponderală (sub 10% din greutatea ideală) în 39,4%. Corespunzător indicelui Harvey-Bradshaw, 27,2% cazuri au fost încadrate ca având activitate ușoară, 43,3% din cazuri ca activitate moderată și 3,9% ca activitate severă; 25,6% din pacienți au fost clasificați ca fiind inactivi clinico-biologic. Din punct de vedere endoscopic au fost descrise ulceratii în 70,6% din cazuri, stenoze în 14,5%, aspectul de „piatră de pavaj” în 18,3%. Distribuția discontinuă a leziunilor a fost menționată la 11,1% din pacienți, fistule non-perineale în 1% din cazuri. Privind clasificarea Montreal, pacienții s-au încadrat în proporții relativ egale între 17-40 de ani și peste 40 de ani. În 56,6% din cazuri localizarea a fost colonică, în 32,2% ileo-colonică și în 11,2% ileală; în 72,2% din cazuri patternul bolii a fost non-penetrant/non-stenozant, în 14,5 % din cazuri stenozant și 13,3% penetrant, afectarea perineală fiind prezentă în 10% din cazuri, dintre care 56% fistule și 44% abcese. **Concluzii** Deși simptomele și semnele la debut, precum și leziunile endoscopice, sunt similare celor din literatură, aspectele clinice identificate confirmă rezultatele studiilor românești anterioare care atestă debutul mai tardiv, localizarea colonică și categoria non-penetrantă non-stenozantă a bolii mai frecvente precum și incidența redusă a afectării perianale. Majoritatea cazurilor noi internate au prezentat forme moderate de BC, urmate în proporții relativ egale de cazurile cu activitate ușoară și în remisiune. Procentul formelor severe de BC a fost foarte redus comparativ cu datele din literatură. Aceste date confirmă existența unui tip particular al BC în România.

## INTRODUCTION

Crohn's disease (CD) is a complex clinical entity, due

to the variability in the anatomical distribution, which causes a variety of the clinical presentation, severity degrees, natural

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history and therapeutic options.

### PURPOSE OF THE STUDY

The aim of our study is to analyze the emerging CD cases in terms of the clinical onset, the Montreal classification, the disease severity and the type of the described endoscopic lesions.

### MATERIAL AND METHOD

The study group consists of 180 adult patients with newly diagnosed CD, investigated in the Clinical Institute of Gastroenterology and Hepatology Fundeni (152 patients) and in the Department of Gastroenterology and Hepatology Timisoara (28 patients), between 2005 - 2009.

For each new cases there were studied the main symptoms and signs at onset, the location and disease behavior and the degree of the disease activity.

The diagnosis was confirmed by endoscopic, radiological and histological examination in the settings of the clinical manifestations.

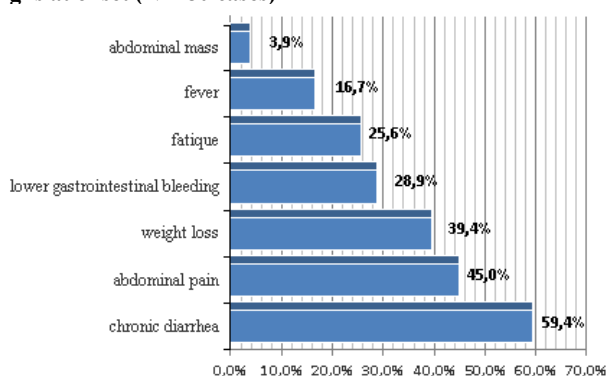
Each case was classified according to age (A), location (L) and disease behavior (Montreal classification).

For assessment of the disease activity we used the Harvey-Bradshaw index (activity index: general well-being 0 = best, 1 = slightly impaired, 2 = very impaired, 3 = severe; abdominal pain: 0 = absent, 1 = mild, 2 = moderate, 3 = severe; number of liquid stools; abdominal mass: no= 0, questionable=1, definite= 2; definite and firm= 3; complications: arthritis/arthritis, iritis/uveitis, erythema nodosum, pyoderma gangrenosum, aphthous stomatitis, anal fissure/fistula/abscess = 1).

### RESULTS

Patients with CD were admitted in the gastroenterology departments with the following signs and symptoms: chronic diarrhea in 59.4%, abdominal pain in 45%, weight loss (less than 10% of ideal weight) in 39.4% and lower gastrointestinal bleeding in 28.9% of cases.

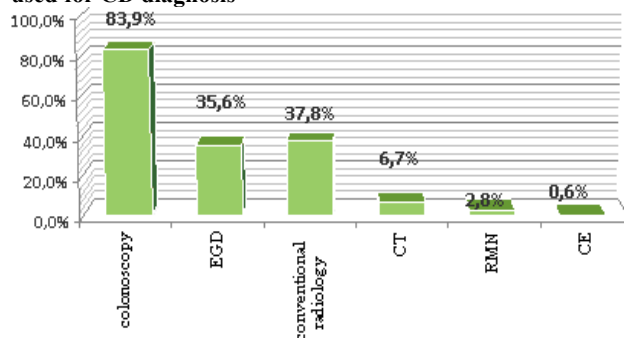
**Figure no. 1. The percentage of the main symptoms and signs at onset (N=180 cases)**



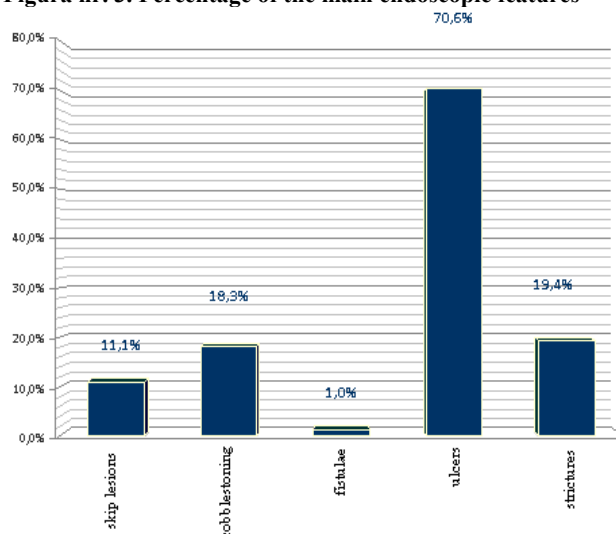
Diagnosis was confirmed by colonoscopy, performed in most cases (83.9%), by esophagogastroduodenoscopy performed in 35.6%, by conventional radiology in 37.8%, abdominal computed tomography in 6.7%, abdominal MRI in 2.8%, wireless capsule endoscopy in 0.6% of cases. The frequency of the procedures used in the diagnosis of CD is shown in figure nr. 2.

Regarding the typical endoscopic features we found: ulcers in 70.6% of cases, stenosis in 19.4%, the "cobblestone" pattern in 18.3%, "skip lesions" in 11.1% of cases, non-perineal fistula in 1% of cases. The frequency of the endoscopic aspects is depicted in the figure nr. 3.

**Figure no. 2. The percentage of recommended procedures used for CD diagnosis**

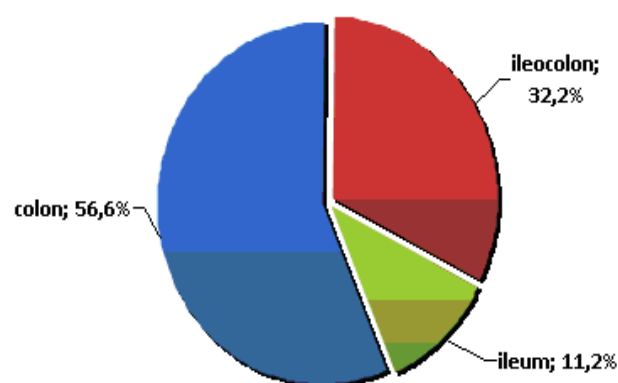


**Figura nr. 3. Percentage of the main endoscopic features**



According to the Montreal classification, 51.7% of patients were aged between 17-40, and 48.3% were over 40; in 56.6% of the cases the colon was affected, the ileocolon in 32.2% of the cases and 11.2% of the cases showed only ileal involvement, the disease behavior was non-stricturing-type/non-penetrating (B1 inflammatory) in 72.2% of cases, stricturing (B2) in 14.5% of cases and penetrating (B3) in 13.3% of cases; perianal disease was present in 10% of the patients (56% fistulas and 44% abscesses). Most common combinations that we have found are: A2L2B1 (23.8%) and A3L2B1 (19.4%) followed by A2L3B1 (8.8%).

**Figure no. 4. The classification of the cases by location**



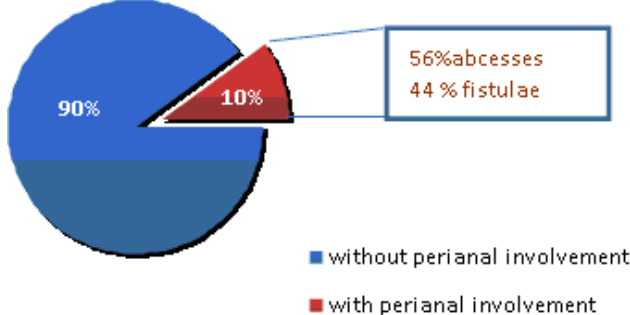
By using the Harvey-Bradshaw index for assessment of the disease activity, we found 43.3% of the cases moderately active CD, 27.2% of the cases mildly active CD, 3.9% of the cases severely active CD, and 25.6% inactive CD.

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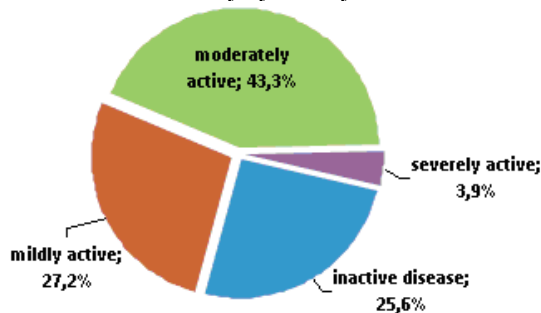
**Figure no. 5. The classification of the cases by behavior**



**Figure no. 6. The perianal involvement**



**Figure no. 7. Disease activity by Harvey-Bradshaw Index**



## DISCUSSIONS

The diagnosis of CD was based on the combination of the following criteria: 1. clinical features: abdominal pain, diarrhea, weight loss (more than 10% from ideal weight) 2. macroscopic features: aphthoid ulcers, deep linear ulcers, ileal disease, rectum typically spared, deep fissures, skip lesions, fistulae, cobblestoning, thickening of the intestinal wall, strictures; 3. radiology: ulcers, fistulae, strictures, cobblestoning; 4. laparoscopic examination: bowel wall thickening, mesenteric lymphadenopathy 5. histopathological examination: focal chronic and patchy inflammation, focal crypt irregularity, granulomas. (1, 2)

In our study the main symptoms were present in a variable rate: chronic diarrhea (59.4%) abdominal pain (45%), weight loss (39.4%), lower gastrointestinal bleeding (28.9%); the frequency of the clinical signs was relatively low, confirming that physical examination may be unnoticed at the onset of the disease in mild forms or during the periods of inactive disease.

According to the literature, chronic diarrhea is the most common presenting symptom of CD, being present in 85% of cases, followed by abdominal pain in 70% of cases and weight loss in 60%. (3, 4)

In this regard, the relatively low frequency of the symptoms in the study group is explained by the high proportion of mildly or inactive CD. Although lower gastrointestinal

bleeding is less common in CD than ulcerative colitis, it is described in literature in 40-50% of colonic CD, explaining the high frequency of this symptom in our study in which the colon was involved in 56.6% of the cases. (2)

Compared with the literature, in our study group the small bowel follow-through was performed in a significantly lower number of cases, while colonoscopy was the gold standard for the diagnosis. (5) Thus, colonoscopy was performed in most cases, esophagogastroduodenoscopy was performed in 34.9% of the cases and small bowel follow through in 39.5% of cases; other imaging techniques (computed - tomography, MRI, capsule endoscopy) were rarely used.

The value of the imaging techniques is high when an extramural complication is suspected (fistulas, abscesses), in the assessment of stricturing, establishing the location and the extent of the disease on the small bowel when endoscopic changes were identified, or the terminal ileum intubation can not be performed. For assessment of the location and of the extension of CD in the small bowel, most centers perform enteroclysis and small bowel follow through; only a few gastroenterology departments are performing enteroclysis CT / MRI. (2)

In Romania the dominant phenotype of CD is inflammatory non penetrant/non stricturing, with mildly and moderately active disease; so, it seems rational that such investigations need to be used with lower frequency when compared with international data. On the other hand, we can speculate that in these conditions, a number of cases with CD with small bowel involvement remain undiagnosed; in the future the more frequent use of CT/RMN techniques will help to refine the CD extension and will change the existing phenotypes.

In our study group the most frequent endoscopic finding was, unsurprisingly, the ulcers (70.6%), followed by "skip lesions", cobblestoning, inflammatory polyps and stricturing.

The initial establishment of the disease location is particularly important since it was described a stability of the anatomical location during the disease evolution in the adult patients, while the disease behavior is dynamic in time. Thus, young patients with ileocolonic location and/or perianal disease who requires corticosteroids treatment for the first attack have a high risk of disabling disease in 5 years from the onset; for these patients the early initiation of immunosuppressant or biological therapy is wholesome. The upper gastrointestinal involvement is encumbered by a more severe prognosis. (6, 7) CD diagnosed under the age of 40 is most commonly associated with ileocolonic involvement, while the incidence of the colonic location increases after 40 years. (8)

The data obtained in our study group is significantly different from those from literature, the ileal location being the most frequent (45%) followed by ileocolonic involvement (25%) and colonic location (25%); the perianal involvement is found in over 50% of the cases, usually in combination with colon locations. (9, 10)

These differences may reflect the particular type of the Romanian patients, but we can not rule out the possibility of underestimating the ileal location because of the lower sensitivity of the conventional radiology in detecting early ileal lesions or merely the more sparsely use of CT/MRI and capsule endoscopy. From this point of view the ileal involvement is likely to be underestimated.

The colonic location was found in similar percentages between 17-40 and after the age of 40, while ileocolonic location was more frequent in patients under 40.

Behavior of CD in the study group was B1 (non-stricturing/ non-penetrating) in 72.2% of cases, B2 (stricturing) in 14.4% of cases and B3 (penetrating) in 13.3% of cases; the perianal disease was present in 10% of cases. These results are

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consistent with previous Romanian studies which also indicated, the non-penetrating/non-stricturing behavior as the most frequent and a reduced incidence of the perianal disease compared with international studies. (11)

The disease activity was assessed by Harvey-Bradshaw index, validated in the pilot and the cohort studies and easier to apply than CDAI score, to which it correlates to 90%. Harvey-Bradshaw Index <5 indicates a clinical remission, between 5-7 mildly active, between 8-16 moderately active and > 16 severely active CD. (12, 13)

In our study group, most cases were moderately active CD (43.3%) and a relative similar percentage being mildly active (27.2%) and inactive disease (25.6%); a low number of patients had severely active CD (3.9%).

Our study confirms previously published data on CD peculiarities in Romania and suggests a mildly onset, non-penetrating pattern/non-stricturing dominant type and the low incidence of the perianal disease. (14)

As the overall incidence of inflammatory bowel disease is increasing in our country, it is expected that, due to lifestyle modification and its proximity to the European Union, the clinical aspects will modify and the cases will be more and more severe.

### CONCLUSIONS

- the main symptoms at onset were diarrhea, abdominal pain, weight loss;
- the gold standard for diagnosis was colonoscopy, performed in 83,9% of the cases;
- the imaging techniques (MRI, CT scan, capsule endoscopy) had a low share in diagnosis;
- the main endoscopic features were ulcers, cobblestoning and "skip lesions";
- the age distribution of the cases was relatively balanced, attesting the late onset of CD compared with literature;
- the disease location was predominantly colonic, followed by ileocolonic and ileal involvement;
- most common behavior was B1, non-stricturing-non-penetrating, with a low incidence of stricturing and penetrating behavior and of the perianal disease;
- most cases were moderately active, followed by mildly active and clinically inactive disease, whereas severely active cases were very low compared with literature data;
- there are still needed extensive multicenter studies for better characterization of phenotype and the evolution peculiarities of CD in Romania.

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