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Romanian Society of Gastroenterology and Hepatology (SRGH)

# The 10<sup>th</sup> National Symposium on Inflammatory Bowel Diseases

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Abstract Book

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# 1 TRANSITION IN IBD - FROM CHILD TO ADULTHOOD

## Daniel Vasile Balaban, Mariana Jinga

As for other chronic digestive illnesses, transition is an important step in the management of patients with inflammatory bowel diseases (IBD). Considering that almost one in four IBD patients are younger than 20 years of age at diagnosis, the magnitude of transition becomes even bigger, and more resources should be focused on successfully getting a patient from a child-centered healthcare provider to an adult-oriented one.

It has been shown in several studies that a well-coordinated transition improves outcomes in these IBD patients and good planning of this process is a crucial prerequisite. It is important to recognize, both for medical professionals and for patients along with 3 their families, that transition is not simply a transfer of care from a health provider to another, but a complex process that addresses medical, psychosocial and educational changes happening when the adolescent becomes a grown-up.

During transition, disease management passes from the parental responsibility to the young adult, who needs to develop skills regarding aspects of the health care system and medical insurance, also knowledge regarding the disease course and complications, medical appointments, IBD medications and tests, fertility issues and lifestyle recommendations. In this setting, transition programs and clinics should be established in communities and strong collaborations among pediatric and adult gastroenterologists should be promoted.

In the current review we summarize the objectives of transitioning, the facilitating and impeding factors for a successful transition process, and also give an overview of the current recommendations regarding transition in IBD patients.

# 2 PATIENT REPORTED OUTCOMES USING THE PGIC SCALE-RESULTS FROM THE MAID COHORT

Mihaela Birligea2, Mara Mitrut2, Theodor Voiosu 1,2, Monica State1, Andreea Benguș 1, Andrei Voiosu 1, Bogdan Mateescu 1,2

# 1- Colentina Clinical Hospital , 2- Carol Davila University of Medicine and Pharmacy

### Introduction

Patient reported outcome (PROs) are reliable instruments that highlight the outcome of treatment and disease management and are increasingly gaining ground in the clinical research field. PGIC (The Patient Global Impression of Change) is a scale that evaluates patient perception of improvement or decline in clinical status following a therapeutic intervention.

#### Patients and method

Prospective data obtained from Consecutive IBD patients enrolled in the MAID cohort and followed annually (with clinical, endoscopic, biologic and histological data at each study visit) was retrospectively analyzed. Quality of life during the study period was assessed using the Short Inflammatory Bowel Disease Questionnaire (SIBDQ) and PRO was measured by PGIC at the most recent timepoint. Our aim was to assess patient perspective on health status changes and establish correlations with objective disease parameters.

#### Results

From a total of 204 enrolled patients, 50 patients with a recent study visit (18 CD, 32 UC) to whom we applied the PGIC were included in the final analysis. 84% evaluated their overall status as very much improved or much improved and only 4% as much worse or very much worse, with a median value of PGIC of 2. SIBDQ scores

#### Conclusions

PGIC results are consistent with a high satisfaction level in an IBD dedicated follow-up program. Quality of life improves over time, reflecting increasing clinical remission rates in the study cohort.

## PREVALENCE AND EVOLUTION PATTERNS OVER TIME OF IRON DEFICIENCY ANEMIA IN ROMANIAN IBD PATIENTS: RESULTS FROM MAID COHORT

Iuliana Bulancea 2, Theodor Voiosu 1,2, Monica State1, Andreea Bengus 1, Andrei Voiosu 1, Bogdan Mateescu 1,2

# 1- Colentina Clinical Hospital, 2- Carol Davila University of Medicine and Farmacy

### Background

Anemia is a frequent occurrence in inflammatory bowel disease (IBD) patients, with several potential and concurrent contributing mechanisms: gastrointestinal bleeding, malabsorption and chronic inflammation. Our main objective is to study the prevalence and evolution patterns over time of iron deficiency anemia (IDA) in Romanian patients with IBD.

### Methods

We conducted a retrospective analysis of prospectively collected data of ulcerative colitis and Crohn's disease patients included in an inception cohort (the MAID study). Clinical data about disease activity and laboratory data (including CBC, serum CRP levels and ferritin levels) was collected at baseline and follow-up visits. We defined anemia according to the ECCO guidelines as hemoglobin levels < 13g/dL for male and 12g/dL for female patients, and iron deficiency using a serum ferritin level < 100 $\mu$ g/ml.

#### Results

168 patients (331 patient-visits) were included in the final analysis; 27 female patients (50%) were anemic at their baseline visit and 67% of patients showed ferritin levels <  $100\mu$ g/ml at baseline.

Overall criteria for anemia were fulfilled at 26.6% of patient-visits, while 71.8% of patient-visits showed ferritin levels < 100ug/ml. Over time, the percentage of patients with anemia significantly improved (27.3% and 16.6% at first and second follow up visits respectively, p=0.048 Chi Square) but iron deficiency as reflected by ferritin levels < 100 did not significantly improve over time (75.6% and 81.8% at first and second FU visits respectively, p=0.119) despite a significant decrease in the proportion of patients with clinical activity at follow up visits (52% at first visit vs 32% at second visit, p=0.001).

#### Conclusions

The prevalence of anemia among IBD patients shows a decreasing trend over time as disease control improves; iron deficiency however remains an unmet problem among a majority of IBD patients despite clinical improvement over time.

## 4 CHARACTERISTICS OF INTESTINAL DYSBIOSIS IN IBD PATIENTS FROM NORTHEASTERN ROMANIA RESULTS FROM A CASE-CONTROL STUDY

Anca Cardoneanu<sup>1</sup>, Elena Rezus<sup>1</sup>, Catalina Mihai<sup>2</sup>, Mihaela Dranga<sup>2</sup>, Iolanda Popa<sup>2</sup>, Raluca Popa<sup>2</sup>, Iulian Bejenariu<sup>2</sup>, Cristina Cijevschi Prelipcean<sup>2</sup>

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#### Introduction:

IBD can be considered the result of the interaction between genetic factors which confer susceptibility and environmental factors that influence the composition of the intestinal microbial flora, thus leading to an abnormal mucosal response. Currently, gut microbiota composition is well known, but its functions have not been fully elucidated.

### **Patients and method**

We conducted a prospective case-control study that enrolled 79 patients between April 2016 to March 2017. The cases were distributed as follows: 20 cases - Crohn's disease (CD), 27 cases - ulcerative colitis (UC), 32 control cases. Intestinal microbiota analysis was performed by real-time polymerase chain reaction (real-time PCR) in the stool samples.

# Results

The diversity of intestinal microbiota was decreased in all cases (CD, UC) compared to control group. The lowest intestinal microbiota was highlighted in patients diagnosed with CD. Patients with UC showed an increased microbial diversity compared to CD. The amount of total bacteria was significantly increased in L3 form of CD (p=0.034). The percentage of Bifidobacterium was higher in L3 form of CD (p=0.010), as well as Lactobacillus group (p=0.023). In UC cases, significant correlations were highlighted only for Bacteroides. In E2 form of UC the quantity of Bacteroides was much higher compared to E3 form (p=0.004). Statistically significant correlations were demonstrated between the CDAI score and the total bacterial group (p=0.023, r= -0.507), respectively Bacteroides (p=0.021, r= -0.511). Significant associations were observed between the Mayo score and Lactobacillus (p=0.000), respectively E. coli (p=0.000).

#### Conclusions

Our results support the presence of a link between intestinal microbial composition and IBD. Intestinal dysbiosis in CD patients has been shown to be the most significant. Cases with UC presented a particular intestinal dysbiosis, different from that of the control group and less pronounced compared to CD.

# 5 THE ARTICULAR INVOLVEMENT IN IBD CAN MODULATE THE COMPOSITION OF INTESTINAL MICROBIOTA?

Anca Cardoneanu<sup>1</sup>, Cristina Cijevschi Prelipcean<sup>2</sup>, Elena Rezus<sup>1</sup>, Mihaela Dranga<sup>2</sup>, Iolanda Popa<sup>2</sup>, Raluca Popa<sup>2</sup>, Iulian Bejenariu<sup>2</sup>, Catalina Mihai<sup>2</sup>

<sup>1</sup>Department of Rheumatology, University of Medicine and Pharmacy "Grigore T Popa" lasi <sup>2</sup>Department of Gastroenterology and Hepatology, University of Medicine and Pharmacy "Grigore T Popa" lasi The study of gut microbiota is a current topic, and new techniques of microbiology and molecular biology have enabled identification of the bacterial species diversity. Intestinal dysbiosis is characterized by an increased intestinal permeability and microbial translocation through the intestinal mucosa, which causes metabolic endotoxemia and systemic inflammation. Many studies have demonstrated the association between gut dysbiosis and various disorders such as inflammatory bowel diseases (IBD).

## **Patients and method**

We conducted a prospective case-control study that enrolled 96 patients between April 2016 to March 2017. The cases were distributed as follows: 20 cases - Crohn's disease (CD), 27 cases ulcerative colitis (UC), 17 cases – IBD + ankylosing spondylitis (AS) and 32 control cases. Intestinal microbiota analysis was performed by realtime polymerase chain reaction (real-time PCR) in the stool samples.

# Results

The intestinal microbial diversity was decreased in all investigated cases compared to the control group. In the studied groups a decrease in the anti-inflammatory bacteria (Bacteroides, C. coccoides, C. leptum and E. coli) was observed, followed by an increase of bacteria having a pro-inflammatory role (F. prausnitzii, Bifidobacterium and Lactobacillus). The most important intestinal dysbiosis was highlighted in patients with CD followed by UC cases. The association between IBD and AS seems to improve the gut dysbiosis. The results on IBD and AS association cases showed a less modified intestinal microbiota, a less significant dysbiosis in these patients. There was a close relationship between disease activity and the degree of intestinal dysbiosis. The higher CDAI and Mayo scores were, the more important intestinal dysbiosis became. Also, the activity scores for AS showed significant correlations with gut microbiota composition in patients with IBD and AS.

#### Conclusions

Corroborating the presented results, we can divide the studied groups, according to the importance of intestinal dysbiosis, into: groups having a significant dysbiosis: CD and UC and the group with an intermediate dysbiosis: IBD+AS. Does the association of IBD with AS can improve bowel dysbiosis in these cases? So far our results support this hypothesis.

## 6 THE IMPACT OF EXTRAINTESTINAL MANIFESTATIONS ON PATIENTS WITH IBD - WHAT SHOULD WE KNOW?

Anca Cardoneanu<sup>1</sup>, Elena Rezus<sup>1</sup>, Catalina Mihai<sup>2</sup>, Mihaela Dranga<sup>2</sup>, Iolanda Popa<sup>2</sup>, Raluca Popa<sup>2</sup>, Iulian Bejenariu<sup>2</sup>, Cristina Cijevschi Prelipcean<sup>2</sup>

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#### Introduction

Patients diagnosed with inflammatory bowel disease (IBD) often develop one or more extraintestinal manifestations

(EIM). From a pathogenic point of view, the occurrence of EIM is due to the implication of an autoimmune reaction to tropomyosin related peptide detected in the skin, joints, eyes, biliary and intestinal epithelium, and due to the presence of a common genetic background, HLA being one of the major associated genetic markers

## Patients and methods

We performed a prospective study that included 517 patients with IBD (Crohn Disease - CD, ulcerative colitis - UC or undifferentiated colitis - NC) diagnosed between 1975 and 2016 in the N-E region of Romania. The patients were extracted from the national database (IBD Prospect). The aims of this study were to: (1) develop specific clinical and epidemiological data on patients diagnosed with IBD who associate EIM, (2) establish the risk factors associated with the occurrence of EIM.

Results: UC cases predominated compared to CD cases (n=368 vs n=135). Only 10 patients were diagnosed with NC. In the study group, 51 cases with IBD and EIM were identified, having a prevalence of 9.9%. Musculoskeletal manifestations were the most common EIM. Peripheral involvement - arthritis (n = 26; 68.42%) predominated, followed by axial damage - sacroiliitis/ankylosing spondylitis (SI/AS) (n =12; 31.58%) (p=0.001). Patients with CD had a 3.48-fold greater risk of developing joint manifestations (p <0.001, OR=3.478; 95% CI 1.779-6.801). In both CD and UC patients, arthritis cases were the most frequent observed (68.42% vs. 31.58%). Patients with CD had a 5-fold higher risk of developing arthritis (p<0.001, OR=5.009, 95% CI 2.21-11.34). Neither CD, nor UC patients, had a confirmed risk of developing SI/AS (p=0.468, OR=1.565, 95% CI 0.463-5.293 for CD) (p= 0.586, OR=0.714, 95% IC 0.211-2.413 for UC). Cases of arthritis and CD (n=16) mainly correlated with the colonic localization of inflammation (n=7, p=0.723) followed by ileo-colonic form of CD (n=7, p=0.321). Patients with arthritis and UC (n=10) initially correlated with pancolitis (n=5, p=0.072, OR=3.023, 95% IC 0.855-10.690) then with proctitis (n =3, p=0.392) and left colitis (n=2, p=0.024, OR=0.196, 95% IC 0.041-0.938).

#### Conclusions

Of all EIM, musculoskeletal manifestations proved to be the most frequent, the results having statistical significance and being consistent with those from the literature. The cases of peripheral involvement (arthritis) predominated, followed by axial damage - SI/AS. Patients with CD had a significantly higher risk.

## 7 INFLAMMATORY BOWEL DISEASE IN ELDERLY: AN OLD PROBLEM IN NEW CLOTHES

Cristina Cijevschi Prelipcean, Mihaela Dranga, Raluca Cezara Popa, Iolanda Valentina Popa, Iulian Petru Bejinariu, Catalina Mihai

Inflammatory bowel disease (IBD) is a chronic inflammatory disease with exacerbations and recurrences. The diagnosis and treatment in elderly patients ("young elderly" 65-75, "middle elderly" 75-85 and "old elderly" > 85 years old), "fit" and "frail" is different and is in fact a challenge. 25-30% of IBD population is over 60; 15% of them were diagnosticated later in life with IBD and 20% had the disease from younger age.

Pathogenesis of IBD in older patients is different. The

genetic factors play a minimum role. Microbiota is now considered to be an important trigger factor by its changes (decrease anaerobes and increase enterobacteria) done by diet modifications, antibiotics and drug use, comorbidities, etc.

In elderly, it is a 6 years delay in IBD diagnostic comparative with 2 years in young patients. If in young patients with Crohn's Disease (CD) the hallmark is fistula and stenosis and colonic involvement is only in 20% of cases, in older patients the main symptoms are rectal bleeding, hypovolemia, anemia and malnutrition. In elderly, colonic involvement is usually lumen limited and occurs in 60% of cases diagnosed over 65. In ulcerative colitis (UC), irrespective of age, the symptoms are the same (diarrhea and rectal bleeding) and the most frequent localisation is left colon.Extraintestinal manifestations are similar irrespective the age with the exception of osteoporosis, more frequent in geriatric population. The differential diagnosis in older patients is very large: from NSAID colitis, ischemic colitis, segmental colitis associated with diverticulosis until infectious colitis, radiation colitis, neoplasm, etc. The evolution and prognosis in elderly depends firstly of delayed diagnosis, comorbidities and infections (especially Clostridium difficile).

In elderly patients the aims of the treatment are to control symptoms, to avoid complications and to improve quality of life, with a great attention to drug-drug interactions. Steroid therapy to induce remission should be strictly monitored and followed, known that 30% of older patients had steroid dependence or resistance and the risks of adverse effects are greater. Budesonide can be an alternative. 80% of older patients with IBD are treated with mesalamine, with attention to nephrotoxicity and minimal secondary reactions (nausea, vomiting, rash, etc). In some patients, thiopurines (azathioprine and 6 mercaptopurine) or methotrexate can be added to mantain disease remission; we have to pay attention to adverse effects of thiopurine ( leukopenia, elevated liver enzymes, acute pancreatitis, elevated risk of lymphoma and nonmelanoma skin cancer). Methotrexat is safer in old patients with fewer and smooth side effects (fatigue, nausea, rash, stomatitis). Biologic agents (tumor necrosis factor alpha, integrin and interleukin antagonists) are less used in elderly IBD because of the high risk of severe infections associated with frequent hospitalisations. We have to say that in the North East Romania, older patients over 60 are treated mainly with mesalamine and very few with immunosuppressive and biologics. These data overlap with those we find in literature.

We must recognize that the diagnosis and treatment of elderly with IBD is a complex problem which needs experience, time and comprehensive knowledge of the disease.

# 8 EPIDEMIOLOGY OF MALNUTRITION IN RECENTLY DIAGNOSED IBD PATIENTS- DATA FROM IBDPROSPECT

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#### Introduction.

Malnutrition affects up to 75% of IBD patients during the course of the disease. It is proven to increase the risk of complications and worsen quality of life. Data regarding nutritional status at initial diagnosis are scarce. We aimed to determine the prevalence of malnutrition in patients recently diagnosed with Crohn's disease (CD) and ulcerative colitis (UC).

## Patients and method.

With the paraclificatione. Prospect multicenter national registry. We selected only new cases, defined as patients who were diagnosed with CD or UC in the last 6 months before inclusion. We defined malnutrition as weight loss of at least 5% of initial weight, during the 3 months prior to diagnosis. [](HEPATIC STEATOSIS ASSOCIATED WITH INFLAMMATORY BOWEL]

#### Results.

Out of the 652 new cases, 381 were UC, 247 CD and 24 were indetermined colitis. Mean age at diagnosis was  $41,9\pm14,8$  years. 54% of patients were male. Malnutrition was found in 33,7% of patients with UC and 42,5% of CD, respectively. After multivariate analysis, in UC malnutrition was associated with male gender (p=0,004) and disease severity (p<0,0001), while in CD malnutrition was associated only with disease severity (p<0,0001).

## Conclusions.

Malnutrition is frequent in IBD patients at disaese onset. Nutritional evaluation and support should be included in the management of IBD patients.

# 9 THE IMPORTANCE OF OPTIMISING ANTI-TNF THERAPY IN IMPROVING THE RESULTS IN ULCERATIVE COLITIS - CASE PRESENTATION

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#### Introduction

There are patients with inflammatory bowel disease whose clinical picture is inconsistent with the biological and colonoscopic picture in terms of severity. According to the biological therapy, the dose intensification should be performed in the absence of a complete therapeutic response and sustained by the determination of specific tests.

#### Material and methods

36-year-old male patient presented: semiformed stools (3-4/ day), diffuse abdominal pain and abdominal meteorism, raising the suspicion of intestinal inflammatory disease. Colonoscopy has found suggestive lesions for the UC pancolic form, and the biopsy confirmed the diagnosis. The lack of therapeutic response at the first stages of treatment (Mesalazina, Prednison, Imuran) required the need for biological therapy (Adalimumab-induction and then maintenance dose-40mg at 2 weeks). After 6 months, clinical remission was obtained, but with biological persistence of the inflammatory syndrome (leukocytosis= 16,000/ mm3 with neutrophilia, CRP accentuation from 0,24mg/dl to 4mg/dl) and increase of faecal calprotectin. Anti-Adalimumab antibodies (negative result) and residual levels of Adalimumab (low) were dosed with the subsequent decision to increase the maintenance dose to 40mg / week.

#### Results

6 months later the patient experienced clinical remission, colonoscopic remission (minimal attenuation of rectal vascular design, normal appearance of the colon) and improvement of the biological picture (normalization of hemoleucogram, decrease in fecal calprotectin).

## Conclusions

Thus, treatment optimization and increased doses of Adalimumab were essential in achieving the therapeutic response (Mayo score improvement from 10 to 1) in this particular UC case where the atypical clinical picture (the absence of blood in the stool) contrasted with the paraclinical one.

### 10 HEPATIC STEATOSIS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE: A SINGLE CENTER STUDY

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## Introduction

The co-existence of non-alcoholic fatty liver disease (NAFLD) and inflammatory bowel disease (IBD) is documented by many recent data. Their importance lies not only in their increasing prevalence but also in the complications that they might cause.

## Methods

We have conducted a single-center study in a retrospective manner. We included 135 patients with IBD and abdominal imaging performed in our institution. Exclusion criteria were: patients with prior liver diseases.

The diagnosis of liver steatosis was performed using abdominal ultrasound and metabolic syndrome was defined according to the National Cholesterol Education Program's Adult Treatment Panel III report (NCEP ATP III) criteria.

#### Results

135 patients were included: 38 patients with Crohn's disease (CD) and 97 with ulcerative colitis (UC). The mean age at diagnosis was 37 years and the sex ratio male/female 1.45 (male/female 80/55).

Abdominal ultrasonography showed liver steatosis in 20% of the patients as follows: 20,6 %; n = 20 in UC and 18,4%; n = 7 in CD. Metabolic syndrome was found in 59,2% (n = 16) of those with hepatic steatosis.

Elevated liver enzymes (ELE) were found in 22,9% of all patients (n = 17).

#### Conclusions

In our study the prevalence of liver steatosis in IBD patients was 20%, which confirms a linkage between metabolic liver disease and IBD. However, in 40,2% of those with confirmed steatosis, metabolic syndrome has not been revealed, aspect that indicates that characteristics of IBD (such as disease activity) might influence NAFLD development.

# 11 CAN THE NEUTROPHIL-TO-LYMPHOCYTE AND PLATELET-TO-LYMPHOCYTE RATIOS PREDICT DISEASE ACTIVITY IN PATIENTS WITH ULCERATIVE COLITIS?

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#### Introduction

For the diagnosis and monitoring of the disease activity of patients with ulcerative colitis (UC), serum biomarkers are generally used, but none of them are specific for intestinal inflammation. Thus, it is desirable in clinical practice to be able to assess disease activity with simple, cheap and objective tools.

The aim of this study is to evaluate if serum neutrophil/lymphocyte (NLR) and platelet/lymphocyte (PLR) ratios are correlated with disease activity in patients with UC.

# Methods

We performed a retrospective study in a tertiary center from Northeastern Romania (January 2015 – January 2017). We included 63 patients with confirmed diagnosis of UC. Patients demographic data, laboratory values, clinical disease activity and endoscopic activity scores were evaluated.

Disease activity was assessed using Ulcerative Colitis Disease Activity Index (UCDAI). We divided the patients in 2 major groups: lot A – patients with endoscopic active UC (Mayo  $\geq$  2) and lot B – patients with endoscopic remission (Mayo 0/1).

#### Results

We included 63 patients (56% men, median age: 33 +/- 6 years). The PLR-ratio was higher in lot A that in lot B (mean 101 vs. 67.1, p = 0,041). Also, disease activity was associated with a higher NLR (mean 5.2 in lot A vs. 1.9 in lot B, p = 0,031).

Regarding the other markers of inflammation: c-reactive protein (CRP) and fecal calprotectin (FC), higher values were also found in lot A compared to those in lot B (median 0,5 mg/dl vs 0,36 mg/dl, p = 0,049; 408 mcg/g vs. 87mcg/g, p=0,014).

FC had stronger correlation with endoscopic disease activity when compared to CRP (sensitivity – Sn: 78%, specificity – Sp: 67%; Sn: 60,4%, Sp: 51%). CRP – was not an independent predictor of active endoscopic disease.

Higher values of NLR and PLR, especially combined, were independent predictors of endoscopic activity. (NLR Sn: 68%, Sp:71%; PLR: Sn:73%, Sp:79%).

## Conclusions

This study highlights the importance of NLR and PLR as useful, inexpensive, safe indicators with direct implications through the correlations between their levels and prediction of active endoscopic disease, especially when used together or with others markers of inflammation (CRP and FC).

## 12 UTILITY OF A SEMI-QUANTITATIVE RAPID TEST IN DIAGNOSIS OF ULCERATIVE COLITIS

Mihaela Dranga1,2, Raluca Popa2, Iulian Bejenariu2, Alina-Mihaela Leustean2, Cristina Cijevschi Prelipcean2, Catalina Mihai1,2

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Background

The aim of this study is to compare two methods for measuring the concentration of faecal Calprotectin (FC) and assess the possibility of distinguishing between ulcerative colitis (UC) and irritable bowel syndrome (IBS).

## Methods

Fifty-three patients with UC and 46 patients with IBS were prospectively included in the study.

All patients were performed colonoscopy to confirm the diagnosis. Faecal calprotectin levels were analyzed by semiquantitative rapid test (CalDetect<sup>®</sup>) and an enzyme-linked immunosorbent assay (ELISA) . Sensitivity and specificity of both assays were calculated.

#### Results

The sensitivity of the test set for direct semiquantitative directly to a value of  $15\mu g / g$  was 78% and specificity of 83% for diagnosis of ulcerative colitis. For the ELISA to a value of 50  $\mu g / g$  sensitivity and specificity were 83% and, respectively 93% (p = 0.068).

#### Conclusions

Although the ELISA test has a higher diagnostic accuracy, it is not significantly higher compared to the semi-quantitative test directly CalDetect<sup>®</sup>). In addition, direct semiquantitative test has the advantage of having immediate results is much easier to use in ambulatory patients.

# 13 MAINTAINING REMISSION IN ULCERATIVE COLITIS: WHAT AGENT TO PREFER?

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#### Background

Inflammatory bowel diseases are characterized by periods of activity and remission. It has been demonstrated that once we achieve endoscopic remission the duration of remission is longer. Aim of the study was to evaluate the effectiveness of various treatments for getting endoscopic remission.

#### Methods

We prospectively evaluated 67 patients with ulcerative colitis who were in remission. Patients were divided into 3 groups: I. maintenance treatment with 5-ASA derivatives, II. maintenance treatment with Azathioprine, III. maintenance treatment with biological agents. Colonoscopic patients were followed for a period of 1 year. Two colonoscopies were performed first at the time of diagnosis, the second clinical relapse or end of treatment in patients who had no relapse during this period. Endoscopic remission was considered at a Mayo endoscopic score  $\leq 1$ .

#### Results

The first group included 23 patients. Of these, endoscopic remission was maintained in the range studied in 8 patients (34.78%). In the second group were 13 patients, 7 patients maintained remission at 1 year (53.84%). The third group enrolled 11 patients, of whom 9 patients maintained remission endoscopic (81.81%) (p = 0.037). In first group, no patient has any side effects. Ingroup two, 1 patient has a mild anemia and in third group one patient has Clostridium difficile infection (p=0.078).

## Conclusions

There was significant differences observed in terms of maintaining endoscopic remission at three treatments studied in favour of biological treatment. Regarding the adverse events there was no significant differences between three groups.

## 14 ULCERATIVE COLITIS: AGE RELATED FEATURES

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## Introduction

The Ulcerative colitis (UC) is a chronic disease with extremely varied clinical manifestations. The purpose of the study was to assess the impact of age on the phenotype and activity of UC. Methods: We It is a prospective study that included 105 patients hospitalized between January 2016 - June 2018. We have noted: age, sex, area of origin, status smoker / nonsmoker, presenting symptoms, presence of inflammatory syndrome, the extension of lesions, severity, treatment, complications, need for surgery. All the patients were examined by colonoscopy and diagnosis of UC was confirmed histologically. The activity of the disease was quantified using Truelove and Witts clinical score of: mild, moderate and severe.

#### Results

Patients were divided into 3 groups according to age: group 1: 51patients ≤ 40 years, group 2: 36 patients, 41-64 years and group 3: 18 patients  $\geq$  65 years. Characteristics of extreme groups were followed by age (young <40 years and elderly> 65 years), to clarify whether there are significant differences between them on UC behavior. At the time of diagnosis 48.5% were younger than 40 years and 17.15% had more than 65 years. In both groups were predominantly men from urban area. The smoking status was more common in younger patients than elderly, but no statistically significant differences (18/51 vs. 6 / 18, p =1). Regarding the symptoms of debut, in the young prevailed diarrhea (younger vs older 41.8% 58.8%, p = 0.09), and in the elderly frankly bloody diarrhea (41.1% vs 66.67% young, p = 0.089). Proctitis was met in 2.94% of the cases (only in the elderly), left-sided colitis as 71.1% - more frequently in young (52.17% vs 18.8%) and pancolitis 26% of cases (29.4% vs 16.66%, p = 0.36). As severity, there is a significantly large number of moderate to severe forms of the young versus elderly (60.8% vs 13.04%, p = 0.028). In all patients had received aminosalicylates, 14, 49 % is the only therapy during follow-up, all elderly patients. The necessary of introducing the immunosuppressive therapies (corticosteroids) and biological therapy was increased in young people with moderately severe forms of disease (corticosteroids: 47, 05% vs 16.67%, p = 0.0270; biological agents: 23.52% vs. 5.55 %, p = 0.0279).

### Conclusion

A more aggressive phenotype with extensive localization of lesions and more severe activity was seen in younger patients. They had an increased need for steroids and biological therapy. Elderly patients experienced mild forms, with limited extension of the lesions, and the majority were able to remain in remission only with salicylates.

# 15 CORELATION BETWEEN DEMOGRAFICA FACTORS AND ACTIVITY OF THE DISEASE IN ULCERATIVE COLITIS

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Rehabilitation Hospital, lassy Ulcerative colitis (UC) is a chronic, idiopathic disease. Although multiple pathophysiological mechanisms have been described, a "trigger" factor could not be determined with certainty Aim: Highlighting the impact of environmental factors on phenotype and severity UC.

#### Matherial and methods

We performed a prospective study lasting three years, January 2016 - June 2018. The study included patients with UC diagnosed and monitored in Center of Gastroenterology and Hepatology, "St. Spiridon " Hospital lasi . All patients were evaluated by colonoscopy to assess the extension of the lesions and biopsies were taken for histological confirmation. UC activity was quantified by Truelove-Witts score.

#### Results

One hundred and five patients were studied. Demographic analysis showed: a predominant male gender (51%), the average age of diagnosis was 42 years, with a bimodal distribution (first peak 18-35 years and another between 55-65 years) without significant differences from the urban than in rural areas. 13.7% had a first degree relative with inflammatory bowel disease (IBD), 31.8% were non-smokers and 24.5% former smokers. To 12.4% of patients the lesions were limited to the rectum, 28.5% had proctosigmoiditis, 30.7% as left colitis and 10.2% lesions were extended to the entire colon. Disease activity was significantly correlated only with the extension of lesions. Gender, age, smoking status / non-smoking, family history of IBD did not influence the activity and extension lesions.

#### Conclusions

The study showed bimodal distribution of age of diagnosis. Environmental factors had no significant influence on the activity or extension of lesions.

# 16 INFLAMMATORY BOWEL DISEASE: CORRELATIONS BETWEEN DISEASE ACTIVITY AND FECAL CALPROTECTIN

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# Introduction

Calprotectina is a polypeptide found in neutrophils and squamous epithelial cells with antimicrobial and antiproliferative activity. The studies have shown that the fecal calprotectin can differentiate between activity and remission in inflammatory bowel disease (IBD). Aim: To assess the efficiency of the dosage of the semiquantitative calprotectin rapid test in evaluating the activity of inflammatory bowel diseases

#### Material and methods

The prospective study included 135 patients with BII (50 with ulcerative colitis, 52 with Crohn disease) hospitalized between January 2016 - May 2017. The diagnosis was confirmed by colonoscopy and histological examination. Fecal calprotectin was measured by means of a semi-quantitative rapid test.

## Results

There were 135 patients with UC and 52 with BC. 61,48% of the UC patients were evaluated during the active disease. 21 of them

had a severe episode of active disease, 48 had a moderate one, while 14 had a mild activity episode. The correlation between the calprotectin values and lesions localization was analyzed, without finding any statistical differences. The data have shown a very strong correlation between the severity of the active disease, assessed through the UCDAI (Mayo) score, and the calprotectin value. In CD' s patients, there were 37 patient with flare. Five patient have severe activity, 18 moderate activity and 13 mild activity. Patients with CD manifested a linear correlation between the severity of the active disease and the calprotectin value.

#### **Conclusions:**

The rapid test for assessing calprotectin could be a useful noninvasive marker in appreciating the severity of clinical and biological disease activity.

## 17 INFLIXIMAB DESENSITIZATION FOR COMPLICATED ENTEROCUTANEOUS FISTULISING CROHN'S DISEASE: FIRST ROMANIAN EXPERIENCE

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#### Introduction

Monoclonal antibodies represent today the most important therapeutic agents for controlling inflammatory bowel diseases, but their usefulness remains limited in some patients due to the development of hypersensitivity reactions. Drug desensitization has proven to be an effective strategy for readministration of a drug which has initially determined a hypersensitivity reaction. Yet, data regarding this strategy for Infliximab is scarce, consisting only of case reports and case series.

#### Case report

We present the case of a 20 years old male patient with longstanding extensive ileo-colonic Crohn's disease, who had recently been operated for drainage of an intraabdominal abcess, developing a complex enterocutaneous fistula. He had been treated at the age of 13 years old for the first time with Infliximab, developping annaphylaxis during the third infusion from the induction of remission protocol. He had been left on cortisone since then, being finally lost to follow-up until his recent surgery. The patient was severely malnourished and suffering from an active extensive ileocolonic penetrating Crohn's disease based on computed tomography imaging. Surgery was not an option due to the nutritional status and extensive disease. We chose Infliximab as the only solution given the prospective data available on fistulising Crohn's disease. We decided to administer Infliximab using the 13-step desensitization protocol (Brennan et al., J. Allergy Clin Immunol 2009) in the intensive care unit of our hospital. We managed to administer the first two infusions of the induction protocol, but the patient developed serum-sickness disease 8 days after the second infusion manifested as severe arthralgia, high CRP and low C3 fraction which contributed to the decision of stopping the treatment.

#### Conclusion

Infliximab desensitization can represent an option for complicated inflammatory bowel diseases in the absence of other drug alternatives. Most hypersensitivity reactions occuring during the desensitization protocol have a lower intensity than the original ones, allowing rapid management and continuation of the treatment.

# 18 PSYCHOLOGICAL SYMPTOMS AND SLEEP DISORDERS IN IBD PATIENTS- IS THERE A CORRELATION WITH DISEASE ACTIVITY?

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# Background

Psychological symptoms(depression and anxiety) and sleep disorders are frequently reported in IBD patients. It is unclear whether sleep fragmentation induces IBD debut or more likely represents a modifiable factor, directly related with anxiety/ depression, potentially contributing to disease exacerbation.

#### Methods

An observational study including 36 IBD patients, followed at 6 months interval, assessed the correlation between depression/ anxiety, sleep quality and disease activity. Hospital Anxiety Depression Score(HADS) (normal values≤7 for both parameters) and Pittsburgh Sleep Quality Index(PSQI) (normal value≤5) were evaluated. Disease activity was evaluated through CDAI/MAYO score, serological markers of inflammation, endoscopic activity.

# Results

89,9% of patients exhibited mild-moderate disease activity at first visit. 85% of patients with recent histological evidence or serological markers of inflammation had abnormal PSQI(mean=8) and HADS(mean=9), independent of clinical disease activity and disease type(p >0.05). There was strong correlation between PSQI and HADS(r= 0.78). 66.67% patients with clinically active disease declared sleep maintanence insomnia, sleep quality being less influenced(21.2%) by IBD-associated digestive symptoms. Second patient visit revealed improved disease activity associated with decreased HADS and PSQI, moderate positive correlation(r=0.43).

## Discussions

Anxiety and depression are associated with poor sleep quality in IBD patients. There is significant association between clinically active IBD and poor sleep quality, anxiety and depression, independent on strcitly disease-related sleeping disturbances and also between psychological symptoms and impaired sleep quality, potentially due to hormonal imbalances and disruption of circadian rhythm.

### Conclusions

IBD and psycological comorbidities are overlapping entities which reciprocally enhance each other, needing multidisciplinary approach and further studies, including eventual correlation with several micronutrient deficits, hormonal imbalance.

# 19 ACUTE INTESTINAL OBSTRUCTION AS AN INITIAL PRESENTATION OF CROHN'S DISEASE

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# Introduction

The prevalence of Crohn's disease (CD) in the elderly population is about 10-15%. Because CD in the elderly is an "unusual" finding, and clinical features can mimic mainly diverticular disease, neoplastic disease or ischemic colitis, a positive diagnosis is often delayed.

## Patients and method

We present the case of a 70-year old female patient, admitted at the hospital with symptoms of bowel obstruction. Her medical history included diabetes mellitus and heart failure. The patient was admitted for nausea followed by vomiting, abdominal pain and lack of bowel movements for 4-5 days prior admission. Abdominal examination revealed the features of acute intestinal obstruction. Abdominal plain X-rays emphasized colonic distention proximal to the transverse colon with distal stenosis. Open right hemicolectomy was performed followed by an anastomosis. Histopathological examination of the resected specimen showed numerous collections of epithelioid cells with giant cells-granulomas. The postoperative period was uneventful. An upper endoscopy was eventually performed and focal gastritis, duodenal ulcers and erythema were identified. Biopsy samples were unremarkable. Treatment with 5-aminosalicylates was started. Initially, remission was induced successfully, however symptoms like persistent diarrhea (6-8 stools/day), diffuse abdominal pain, and rectal bleeding required the use of systemic corticosteroides and immunosuppressant therapy were started, with a good clinical response.

### Conclusion

Elderly-onset is uncommon for CD and clinical features are nonspecific. CD should be taken into account as one of the causes of a surgical abdomen. Involvement of the upper gastrointestinal tract is uncommon, nevertheless the endoscopic findings may be used to discriminate between CD and ulcerative colitis.

## 20 PULMONARY MANIFESTATIONS OF INFLAMMATORY BOWEL DISEASE OR LATENT TUBERCULOSIS?

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# Introduction

Crohn's disease (CD) is an inflammatory disorder characterised by an inappropriate response of immune system. The abnormal host immune response of these patients in association with the immunosuppressive therapy increases the risk for infection.

# **Patients and method**

We present the case of a 42-year old female patient admitted in our hospital and diagnosed as case of intestinal obstruction. Exploratory laparotomy was performed and diseased resected segments (ileocolonic anastomosis) were confirmed as CD on histopathology. A thorough evaluation of active or latent infections was performed, and the patient was eventually started the anti-TNF therapy regime. Seven months later, the patient began having low-grade fever (37.4-38.0°C), usually in the afternoon, fatigue, anorexia, productive cough, without respond to medical treatment. A new evaluation revealed a left pulmonary mass which proved to be active tuberculosis. Purified protein derivative tuberculin (PPD) test was strongly positive, and positive cultures for Mycobacterium tuberculosis confirmed the diagnosis. The anti-TB treatment with Isoniazid, Rifampicin, Streptomycin and Ethambutol was initiated and shortly after, clinical evolution was worsted by persistent diarrhea (>20 stools/day), weight loss (10 kg), and mushy stool that occasionally contained mucus, accompanied with periumbilical and the right abdominal dull pain, resulting in developing of malnutrition syndrome due to the side effects of the medication. The intravenous method proved effective and lead to resolution of TB infection.

## Discussion/Conclusion

A good interdisciplinary collaboration results with well outcome of patient with resolution TB infection and reduction of CD's activity. Treatment for TB, if suspected, should be empirically instituted with a full course of anti-TB agents.

# 21 THERAPY EXPERIENCES AMONG PATIENTS WITH INFLAMMATORY BOWEL DISEASE-RELATED IRON DEFICIENCY ANEMIA - A REAL LIFE STUDY

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# Background

The leading cause of anemia in patients with inflammatory bowel disease (IBD) is iron deficiency. Intravenous iron is the first-line treatment for clinically active IBD or previous oral iron intolerance. The aim of our study was to evaluate the therapeutic approach of iron deficiency and delivery either intravenously (i.v.) for iron ferric carboxymaltose (FCM) and iron-sucrose complex (IS) or oral preparations for iron deficiency anemia associated with IBD.

### Methods

We retrospectively analyzed patients with IBD-related iron deficiency anemia, hospitalized in a tertiary center in North-Eastern Romania between January 1, 2016 through December 31, 2017. Diagnosis of IBD was established based on endoscopic and histological findings, with biologically documented anemic syndrome (Hb<13 g/dl for males and <12 g/dl for females, MCV< 78/fl, MCH< 27/ pg, iron status – sideremia <50mcg/dl). The administration of iron preparations (i.v., oral) was based on the individual clinical factors (the degree of anemia and disease severity) and improvement in hematological parameters as well as the frequency of adverse effects were analyzed.

## Results

The study included 34 patients with IBD-related iron deficiency anemia, mainly males (21 - 61.76%), with mean age 44.8±12.8 years. Twenty (58.82%) patients had severe anemia (Hb<8g/dl) and received i.v. iron preparations in the form of iron-sucrose complex (13- 65%) or ferric carboxymaltose (7 - 35%), and the remaining 14

(41.17%) patients received oral iron preparations. For all patients, the mean value of hemoglobin at admission was  $8.2\pm1.1g/dl$ , with lower value in patients requiring i.v. iron preparations. Nine (64.2%) patients with oral iron administration had adverse effects (headache – 3, nausea - 5, constipation – 1) while 6 (30%) patients with i.v. preparations had headache (4 – 66.6%) and injection site reactions (2 – 33.3%). Mean hemoglobin value at discharge was 12.4±1.3g%, with no significant differences (p = 0.063) between patients receiving either i.v. or oral preparations.

#### Conclusion

Most patients with IBD-related iron deficiency anemia required parenteral iron preparations. Intravenous administration represented a more rapid achievement of Hb with significantly lesser adverse effects compared to oral administration.

# 22 INFLAMMATORY BOWEL DISEASE AND VASCULAR COMPLICATIONS

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#### Introduction

Patients with inflammatory bowel disease (IBD) have an increased risk of vascular complications. Systemic inflammation rises both risk of arterial (ATE) and venous thromboembolisms (VTE) and complicating the course of IBD and can lead to significant morbidity and mortality.

#### Methods

We conducted a retrospective study including all patients hospitalised for IBD in the Institute of Gastroenterology and Hepatology Iasi between June 1, 2012 and June 9, 2017.

#### Results

238 of IBD patients – 146 (61%) with UC and 92 (39%) with CD who have been treated in Institute of Gastroenterology and Hepatology lasi were analysed retrospectively. The diagnosis of thromboembolic complication was confirmed with appropriate diagnostic methods (color doppler ultrasound or CT angiography). A venous thromboembolism occurred in 8 patients (3.36%), 5 men and 3 women. Moreover, 5 patients had Crohn's disease and 3 had ulcerative colitis. All of them had moderate or severe activity, 6 patients were under corticotherapy and 2 under biological therapy. It was a deep thrombosis in 6 patients and associated with pulmonary embolism in 1, as well as 1 with cerebral venous sinus thrombosis, and a portal vein thrombosis in 1.

#### Conclusion

IBD patients are at an increased risk of sustaining VTE and increased risk of VTE-related mortality when compared with non-IBD patients. IBD activity is an independent risk factor for VTE development.

# 23 SERUM LEVELS OF IL-17 AND IL-23 AND IBD SEVERITY ASSESSMENT IN CLINICAL PRACTICE

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#### Background

Interleukin-17 (IL-17) and Interleukin-23 (IL-23) play a critical role in inflammatory bowel disease (IBD) immune response. We aimed to investigate if the serum levels of IL-17 and IL23 among IBD patients reflect disease severity and if they correlate with standard inflammatory biomarkers (CRP, calprotectin).

#### Methods

We prospectively included in the study 62 IBD patients and 15 healthy controls. According to disease activity scores, we further classified the patients into severe and mild/moderate disease (CDs, CDns, Ucs, Ucns). Serum levels of IL-17 and IL-23 were determined using ELISA assays. We used Mann Whitney U test for distribution among groups, and Spearman's rank correlation for describing relationship among variables. Numerical data was presented with median and interquartile range.

### Results

In CDs patients, IL-17 had with 930.48pg/mL higher serum levels than CDns group, p=0.119. As for IL-23, CDs group had with 699.86pg/mL higher serum levels than mild/moderate group, p=<0.001. In UCs patients, serum levels of IL-17 were with 1328.13pg/mL higher comparatively to the mild/moderate group (p=0.003), and for IL-23, with 723.62pg/mL higher in the UCs group (p<0.001). Spearman's correlation test between IL-17, IL-23 and Fcal showed a coeficient of 0.52 for IL-17 (p=0.003) and 0.67 for IL-23 (p=<0.001). The median distribution of IL-23 serum levels according to intestinal complications showed with 622.1pg/mL higher values in fistula group (p=0.035).

#### Conclusions

IL-17 and IL-23 serum levels can differentiate between IBD patients with severe and non-severe disease. Further monitorization of these cytokins in larger IBD groups might be a promissing tool in assessing disease progression.

## 24 THE FREQUENCY OF ADVERSE EVENTS DURING ANTI-TNF THERAPY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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#### Indroduction

In recent years, treatment of inflammatory bowel diseases (IBD) has witnessed great advance as a result of anti-TNF therapy. However, side effects may occur at any time during the treatment, sometimes leading to severe complications and discontinuation of the treatment.

#### Aims

The aim of our study was to determine the frequency of anti-TNF therapy side effects in a group of patients with IBD from a tertiary center in North Eastern Romania.

#### Methods

We conducted a single center retrospective study, including

patients with diagnosed IBD that were receiving biological therapy (Infliximab or Adalimumab), admitted in our Gastroenterology department during a period of 3 years (June 2015 – June 2018). Demographic, clinical characteristics and laboratory findings were collected from medical records.

## Results

A total number of 32 adult IBD patients (18 CD, 14 UC) treated with anti-TNF agents were included in our study: 19 received adalimumab and 13 infliximab. The mean age at induction was 34.1 (19-58 years) and the median duration of the disease was 10±4 years. Overall, adverse effects were noted in 8 patients: 4 developed non-severe infectios pneumopathy managed with antibiotics; one patient treated with adalimumab developed paradoxical psoriasis; immediate hypersensitivity reaction was observed in 2 patients treated with infliximab; one patient treated with Adalimumab developed plumonary tuberculosis and needed discontinuation of the treatment.

# Conclusion

Anti-TNF therapy has an important place among the therapeutic 26 arsenal of IBD patients. Careful monitoring is necessary due to its side effects that can sometimes be severe, requiring discontinuation of the treatment.

# 25 FISTULISING CROHN'S DISEASE TREATMENT – REAL LIFE DATA

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Key words

Crohn's Disease, Fistulae, Treatment

# Introduction

Fistulising Crohn's Disease is a very disabling manifestation and source of morbidity for Crohn's disease patients. Currently treatment options include medical treatment, surgical interventions or combined medical and surgical treatments. Perianal disease may precede intestinal symptoms, appear at the time of diagnosis, or later on. The aim of this study is to observe the outcome of the treatment for fistulising Crohn's disease in our department.

## Methods

We evaluated 85 patients with Crohn's Disease admitted in Fundeni Clinical Institute in Gastroenterology II Department during 2015-2017. We selected the patients with penetrating Crohn's disease.

### Results

18.82% (n=16) of the patients with Crohn's Disease admitted in our department had fistulising CD. Men were the majority of the patients (62.5%), with the mean age of  $36.25\pm12.5$  years.

50% of the patients presented perianal fistulae. The rest of the patients had non-perianal fistulae: 18.75% of them had enteroenteric fistulae, 37.5% entero-cutaneous fistulae and one patient with entero-vesical fistula .Out of the patients with enterocutaneous fistulae 50 % had spontaneous fistula and 50 % postsurgical fistula. Antibiotics as an adjuvant therapy were used on 56.25% of patients who had associated abscess.

The majority of the patients (75%) had active transit of the fistulae at the diagnosis. At the moment of the diagnosis 31.25% of the patients were on azathioprine treatment, 18.75% on infliximab, one was on adalimumab and one on combo therapy with azathioprine

## and infliximab.

62.5% of the patients at the diagnosis were assigned to receive combo therapy, but not all of them had decreased fistula drainage or fistula closure on it. Surgery was performed on 68.75% of the patients (drainage, fistulectomy, ileal resection, enterectomy, setone). One patient had fistula closure with adalimumab and surgical drainage.

The mean period to fistula closure was  $14.93 \pm 9.74$  months, the fistula closure being succeeded at 56.25% of the patients.

## Conclusions

All non-perianal fistulas were treated with combo therapy with azathioprine and infliximab with positive results. Half of the patients with non-perianal fistula had prior surgery. Loss of response to infliximab and azathioprine developed in 3 patients in an average of 6.46 months. The treatment of fistulas is difficult and always require multidisciplinary teamwork.

## 26 PERICARDITIS DURING INFLIXIMAB ULCERATIVE COLITIS REMISSION INDUCTION - CASE REPORT

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## Introduction.

Biological therapy is an important tool in inflammatory bowel disease (IBD) management.

Patient and results (case report). This is the case of 40-year-old man known with a 4 years history of left sided ulcerative colitis.

•At T minus 12 months - patient in remission under 40mg adalimumab s.c. every two weeks.

•At T minus 6 months - loss of response, adalimumab dose escalation (every week).

•At T minus 3 months - loss of response, with moderate severity flare. Colonoscopy - left sided colitis, Mayo endoscopic score 2-3. Pathology - active disease, no CMV infection. Serology and stool tests - no CMV infection, no Clostridium difficile infection, no parasites. Quantiferon test negative. Stop adalimumab and successful remission with oral methylprednisolone (1mg/kg) and azathioprine (2mg/kg).

•At T minus 2 weeks symptoms reappear after steroid tapering (steroid dependence). Start infliximab 5mg/kg 0,2,6 remission induction schedule. Pursuit of azathioprine (2mg/kg).

•At T minus 3 days the patient experience repeated fever and chills.

•At T time (the moment of the scheduled 2nd infliximab infusion) - urine, stool, chest X-ray, sputum cultures, abdominal ultrasound all normal. Slightly raised pro-calcitonin. Trans-esophageal heart ultrasound and CT scan - minimal pericardial effusion. Start oral levofloxacin for 7 days and pursuit of scheduled infliximab and azathioprine. After one week no symptoms, normal pro-calcitonin, no pericardial liquid. Quantiferon eventually negative.

Remission was obtained and is currently maintained with 5mg/kg infliximab every 8 weeks

## Conclusion

Care must be taken to screen and supervise patients under IBD biological therapy for infectious complications.

# 27 NEUROENDOCRINE CELLS DENSITIES ALTERATIONS IN COLONIC MUCOSA OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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## Introduction

Several published studies on human and animal models showed increased densities of NEC in colonic mucosa of inflammatory bowel disease (IBD) colitis compared to non-IBD controls.

The aim of our study is to determine de NEC densities in colonic mucosa of patients with IBD in our Department.

## Methods

Colonic biopsies from 11 patients with IBD and 11 patients screened for colorectal cancer were evaluated histopatological with hematoxylin-eosin staining and immunochemical with chromogranin A (CgA) and synaptophysin antibodies (Syn). We assessed the number of NEC by manual counting at optic microscope on 10 oriented crypts and 20 transverse sectional crypts.

## Results

In IBD group NEC had a patchy and superficial distribution, organized in groups or nodules of 3 to 6 hyperplastic cells/crypt with a mean density of 3.16 CgA positive and 2.54 Syn postive NEC/ crypt in IBD group compared to 1.7 CgA positive and 1.28 Syn positive NEC/crypt in non-IBD controls; P=0,0001, P=0,002.

When compared to IBD duration, NEC densities decreased with IBD evolution so that in patients with IBD duration between 1 and 5 years mean NEC densities were 3,4 NEC/crypt (CgA )and 2.8 NEC/crypt (Syn) compared to 2,76 NEC/crypt and 1,72 NEC/crypt respectively in patients with disease evolution longer than 5 years; P=0,19, P=0,14.

There are no significant differences between NEC distributions in active versus inactive disease with a mean density of 2,3NEC/crypt (CgA) and 3 NEC/crypt(Syn) in active IBD colitis and 3 NEC/crypt (CgA) and 3.5 NEC/crypt (Syn) in inactive colitis; P= 0,1 and 0,2 respectively.

## Conclusions

Our study showed an increased density of CgA and Syn positive NEC in patients with IBD. We observed a decreased in NEC densities with IBD evolution possibly related to IBD treatment.

### Key words:

neuroendocrine cells hyperplasia, inflammatory bowel disease

## 28 OUTCOME OF ANTI-TNF DISCONTINUATION IN PATIENTS WITH IBD: A PROSPECTIVE OBSERVATIONAL STUDY ON A SERIES OF CASES

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## Introduction

Anti-TNF therapy can be stopped in inflammatory bowel disease (IBD) patents with sustained clinical remission at 1 year. 50% of patients relapse at 1 year and more than 80% achieve the response and have no adverse events after restarting the same anti-TNF agent.

### Patients and methods

We performed a prospective observational study on a number of 11 patients with IBD: 4 with Crohn's disease (CD) and 8 with ulcerative colitis (UC) in whom we stopped anti –TNF therapy for sustained clinical and endoscopic remission. All patients were treated with anti-TNF therapy in monotherapy and were in sustained clinical and endoscopic remission for a mean period of 4,72 years range

(2-8). All patients were dees calated on conventional treatment and followed on a mean period of 9,63 months (range 5-19 ).

## Results

9 patients (81.8%) maintained clinical remission on a mean period of 10.55 months. Two patients relapsed at 5 and 9 months respectively. One patient who relapsed had therapeutic drug level before stopping the anti-TNF agent . Retreatment of relapse with the same anti-TNF agent was effective (both patients responded) and safe.

## Conclusion

We evaluated a series of 11 cases with IBD in whom we stopped the biological agent for sustained clinical and endoscopic remission. 81.8% of patients maintained long-term clinical remission. Retreatment with the same anti-TNF agent was safe and effective.

## Discussions

Predictive factors of relapse are needed for the optimal selection of patients in whom stopping the biologic is safe for long term maintained clinical remission.

# 29 NEW EPIDEMIOLOGICAL DATA IN NORTH-EAST ROMANIA -IBD PROSPECT

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Inflammatory Bowel Disease (IBD) has an incidence and prevalence increasing in recent years; the environment factors seem to have a decisive role in epidemiological changes. In Europe there is a west-east gradient of IBD, with an incidence of 2.1 times higher for Crohn disease (CD) and 1.9 times higher for ulcerative colitis (UC) in Western countries compare to Eastern countries. Epidemiological data shows a tendency of increasing incidence and prevalence of IBD in the east of Europe, as a result of adopting the western style of life.

IBD Prospect started in Iasi in 2011 and now there are 664 patients enrolled, which represent more than 20% of all registered Romanian IBD Prospect patients. Most patients (more than 70%) have UC; this data confirm previous studies which revealed a higher incidence of CD in south-west vs higher incidence of UC in northeast Romania. Comparing 2011 and 2018 we observed a tendency of increasing CD cases. The mean age of IBD diagnose was 43 years, with a slightly male predominance both in UC and CD. The family aggregation was lower than in other European cohorts, and 10-15% of patients were active smokers with no difference between UC and CD. According to Montreal classification in CD B2 and L2 were more frequent; in UC the most frequent location was E2. The majority of patients (80%) had mild and moderate activity. Intestinal complications were found in 12% and extraintestinal manifestations in 14%, both more frequent in CD compare to UC. 15% of patients had Clostridium difficile infection, and approximately 40% anemia (most common iron deficency anemia). More than 20% of patients were treated with biologics; it was a gradually increase in biologic use from 2011 to 2017.

In conclusion in North –East of Romania we still have more UC than CD, more anemia, less intestinal and extraintestinal complications, but it is a slow tendency of increasing CD cases, moderate and severe forms and biologics use.

# 30 EXTRAINTESTINAL MANIFESTATIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)

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## Background&Aim

Patients with IBD often associate extraintestinal manifestations (EIMs), some of which being occasionally real medical challenges regarding diagnosis and therapeutical management. The aim of our study was to evaluate the frequency and type of EIM in ulcerative colitis (UC) and Crohn's disease (CD)

## Methods

Consecutive patients with a definitive diagnosis of IBD hospitalized in our institution between January 01, 2016 and August 01, 2018 were included. Demographics, type and chronology of EIM, as well as clinical course of IBD, were assessed.

### Results

Ninety-seven patients with IBD (50 UC, 47 CD) with a mean age of 41+11 years, predominantly females (58%) were analyzed. EIMs were identified in 29 patients (30%); out of them, 11 patients (38%) had arthropathy, 5 (17%) had aphtous stomatitis, 9 (31%) had cutaneous manifestations (3 had erythema nodosum and 6 pyoderma gangrenosum), 2 (7%) had primary sclerosing cholangitis, 1 (3.5%) had ophthalmological manifestations, and 1 (3.5%) cardiopulmonary manifestations. The EIMs were diagnosed after the IBD diagnosis in 80% of the patients, and the remaining of 20% cases were diagnosed either before (3%) or concomitant (17%) with the diagnosis of IBD. In 43% of all cases, treatment was intensified because of the development of EIMs.

## Conclusion

Articular manifestations were the most common EIM in our cohort. EIMs were predominantly diagnosed after the diagnosis of IBD, but there should be an increased attention because of the possibility to develop EIM before the diagnosis of IBD.

## Keywords

inflammatory bowel disease, extraintestinal manifestations

# 31 CALPROTECTIN TESTING: EASIER SAID THAN DONE

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### Aim

The idea of this study emerged at a discussion with British colleagues who declared they have encounterd extremely low compliance to calprotectin testing in their outpatients.

We decided to prospectively investigate the level of compliance with fecal calprotectin testing in our cohort of inflammatory bowel disease patients.

### Methods

Several methods are currently used. We prescribed only quantitative assays, in hospital or ambulatory.

All consecutive adult inflammatory bowel disease patients having

been prescribed an fecal calprotectin testing starting July 2017 were included.

They been instructed about calprotectin importance to the follow up and clinical decision in their disease and of the necessity of bringing the test result.

At their next two visits to the hospital, patients had to return the result of the fecal calprotectin test and to answer to a simple questionnaire: 'Have you brought the result as required? If not, why not? If so, did you encounter any difficulties when collecting the sample?

## Results

Fifty-five patients were included (19 women; 31 patients with Crohn's disease). The mean age was 41 years (21–81). Thirty-five (64%) had performed the fecal calprotectin test.

Of the 20 patients who did not take the test, the prime reasons for non-compliance were forgetfulness (9), refuse to do the test (4), constipation (2), refuse to handle feces (2). In three patients' difficulties collecting the stool sample were the main reason of failure (laboratory refused the vials that contained more material than needed). Although it is a small number of patients no difference was observed in terms of sex and age in non compliant patients. Cost might be a problem since not in all patients the test was supported by industry with vouchers and the implementation of the gratuity in the national health program is far from optimal.

## Conclusion

More than half of the patients performed the faecal calprotectin test. The main reason for non-compliance was forgetfulness or refusal.

We believe that there is a need for better patient education on the paramount importance of the fecal calprotectin testing in monitoring IBD.

# 32CAPSULE ENDOSCOPY IN A TREAT TO TARGET APPROACH TO CROHN'S DISEASE PATIENTS

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## Background:

In recent years a proactive attitude is getting more common in treating inflammatory bowel disease (IBD) patients. We now look beyond symptoms and imaging, biomarkers and drug monitoring help guide the treatment changes.

This strategy that is based on regular assessment of disease activity by using objective clinical, imagistic and biological outcome markers and the subsequent adjustment of treatment is called "treat to target approach".

Capsule endoscopy has a well definite role in Crohn's disease patients' diagnosis and monitoring. We present our experience of capsule endoscopy use in Crohn's disease patients monitored in a treat to target manner.

#### Methods:

We prospectively evaluated 17 Crohn's disease patients followed in proactive manner using fecal calprotectin in a single center.

Rapid reader 8 software and Pillcam colon 2 capsule were used in the study. A panendoscopy examination was realized setting the capsule to record before swallowing it.

#### **Results:**

Seventeen patients with known Crohn's disease had at least a panenteric endoscopy. Five of them had 2 successive examinations and one had 3 complete examinations.All patients had high levels of fecal calprotectin, but only 13 of them had symptoms. We had an

#### The 10th National Symposium on Inflammatory Bowel Diseases

incomplete examination due to capsule retention in the ileum for 9 hours. Active lesions were found in 15 patients: two of them had ileo-colic ulcerations, one had gastro-duodenal and ileal lesions, one had a peri-anastomotic fistula and 11 patients had ileal disease. Two patients had no lesions. Pan-enteric endoscopy examination identified lesions in 88% of patients with raised fecal calprotectin (even in asymptomatic patients).

In those who had more successive examinations, the use of capsule proved to be useful for the therapeutic decision, leading to interruption of treatment in 1 patient (with 3 examinations), switch to biologic therapy in 2 patients and administration of budesonide in the rest of them.

#### Conclusion:

In selected Crohn's disease patients (inflammatory pattern) without known/suspected stenosis the pan-enteric endoscopy using colon capsule might be used in conjunction with biomarkers to actively monitor the patients in a treat to target approach. This helps to stratify disease activity (due to well known limitations of clinical assessment) and can be paramount to guide therapeutic modifications. Still, it is an expensive tool not supported by national insurance programmes, hence with reduced availability.

The newly designed Crohn's capsule, due to its software is more adapted for successive, comparative examinations and seems to be a promising tool for disease monitoring.

## 33 STEROID ASSESSMENT TOOL (SAT)-A USEFUL INSTRUMENT TO IMPROVE QUALITY OF CARE IN IBD PATIENTS

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#### Introduction

According to guidelines, patients should be able to access the same standard of care irrespective of where they live or are treated.

In reality, there are notable variations in IBD patient's care. This is influenced by local standards of treatment, payer preferences, adherence to guidelines, patient and physician preferences and ultimately access to a center where all these are taken into account and applied by specialized personnel.

Significant differences exist between centers and tools to asses the performance and adherence to guidelines and permanent auditing is performed. Steroids remain the mainstay of treatment for patients with an exacerbation of inflammatory bowel disease (IBD). However steroid use as maintenance therapy is limited by terrible side effects or long-term complications (infections, Cushing syndrome, hypertension, diabetes mellitus, osteoporosis and aseptic necrosis of bone) (1).

The European Crohn's and Colitis Organisation (ECCO) define steroid excess as disease requiring more than two steroid courses within the previous 12 months or a new disease flare when trying to taper steroids or within 3 months of stopping steroids (2,3). In an effort to optimize the use of steroids in the treatment of IBD in the United Kingdom, the collaboration between 14 IBD consultants and nurses and AbbVie in 2014 resulted in the development of a secure web-based steroid assessment tool (SAT), enabling clinicians to monitor steroid use within their own clinical setting.

Several British studies were then published using SAT as a tool to assess the quality of care offered in different centers or nationwide (4).

Iterative comparisons in the same center are possible and also comparing local practice with national data can lead to a modification of care and better implementations of ECCO guidelines.

#### Aim

The goal of our project was to audit our center on the use of steroids for IBD treatment and to initiate appropriate changes to improve IBD patient quality of care.

#### Methods

We used SAT in fifty-five consecutive patients seen in our unit in June and July 2018.

#### **Results and discussion**

We included 55 patients (19 women) with mean age of 41 years. The majority (31) of patients had Crohn's disease. The number of patients with excess steroid use is 14%. The data from the UK national survey showed a 13.8% excess use, so our center data are comparable (4). Another study from Scotland with a comparable number of patients (43) showed a 16% excess steroid use (5).

In this study the majority of patients receiving steroids were coprescribed bone protection medication. In our cohort none of the patients which were prescribed steroids received bone protection medication, irrespective of age, sex or disease type which is quite a surprise.

#### Conclusion

Steroid assessment tool (SAT) proved to be very useful and easy to use instrument in real life settings.

After using SAT appropriate changes in our practice were planed and discussed with our physicians and nurses especially in limiting the steroid excess and about the paramount importance of coprescribing bone protection medication while on steroids. A new assessment of our patients is planned in six months.

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# 34 FREQUENCY OF UROLITHIASIS AS AN EXTRAINTESTINAL MANIFESTATION OF INFLAMMATORY BOWEL DISEASE IN A TERTIARY CENTER FROM NORTH-EAST ROMANIA

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#### Background

Extraintestinal manifestations (EIMs) of inflammatory bowel disease (IBD) are common in both ulcerative colitis (UC) and Crohn's disease (CD). The association of IBD with complications in the urinary tract has been reported in many studies with urolithiasis being a common manifestation. The aim of this study was to assess the frequency of urolithiasis and urinary tract infection in IBD patients.

#### Material and Methods

We conducted a descriptive cohort study with prospective data collected from all patients with IBD admitted to Institute of

Gastroenterology and Hepatology lasi, between January 1, 2011 to 36 June 30, 2016. Demographic data and clinical characteristics were reviewed.

## Results

The study population included 329 IBD patients (mean age 44.11 $\pm$ 15.51 years), predominantly male patients (58.9%). A total of 228 (69.3%) were diagnosed with ulcerative colitis (UC) and 101 (30.7%) with Crohn's disease (CD). The study group consisted of predominantly left-sided colitis (51.7%) and colonic CD cases (43.5%). We found a number of 22 (6.7%) patients with IBD and urolithiasis. Amongst them, 15 (49.3%) had UC and 7 (23%) had CD. Moreover, we identified 21 (6.3%) patients diagnosed with urinary tract infection, most of them (66.6%) being with UC.

## Conclusion

Urolithiasis is the most common urinary complication in patients with IBD. While urinary tract manifestations are more common in patients with CD, in our study these manifestations were predominantly diagnosed in UC subgroup.

Often clinically underestimated, urologic complications in IBD patients are not rare and need to be correctly recognized in order to receive appropriate management.

## 35 CLOSTRIDIUM DIFFICILE IN INFLAMMATORY BOWEL DISEASE RELAPSES

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### Introduction

The similar clinical and biological picture between inflammatory bowel disease (IBD) acute relapses and Clostridium difficile (CD) infection makes the differential diagnosis difficult. The objective of this study was to evaluate the prevalence and predictors of CD infection in patients with IBD.

#### **Patients and method**

We examined the records of 94 patients with IBD acute relapse for which the presence of CD toxins was determined by immunochromatographic assay. We collected disease's history data, 37 results of the immunochromatographic tests and the administered therapy. We tested the correlations using Chi-square and t tests. Logistic regression analysis was used to identify the predictors of enteric infection.

#### Results

Of the 94 immunocromatographic tests recommended during acute relapses, 14.2% were positive for CD. Personal history positive for CD infection and IBD with colonic involvement are risk factors for CD infection, while previous surgery is a negative predictor for CD infection. Most patients with CD (65.9%) were treated with vancomycin. CD patients required a longer period of hospitalization (7 vs. 4 days, P = 0.034). Patients without CD infection were more likely to benefit from changes in the therapeutic regimen for IBD (P = 0.012).

#### Conclusions

Assessing the presence of CD infection should be considered during any IBD relapse, given the high rate of infection and the different therapeutic measures to be applied.

# COLORECTAL CANCER AS AN INFLAMMATORY BOWEL DISEASE COMPLICATION: PATIENTS AWARENESS

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## Introduction

Our aim was to evaluate the inflammatory bowel disease (IBD) patients awareness of the risk of developing colorectal cancer (CRC) as a disease complication.

#### Material and Methods

150 IBD patients (84 with ulcerative colitis - UC), from "St. Spiridon" Hospital, Iasi, Romania – Gastroenterology Department, were asked to answer a set of specific questions. The questions included details about the particular aspects of CRC risk in IBD according to the latest guidelines: risk factors (age at diagnosis, disease duration), best screening method, the moment when screening should start, therapeutic options etc.

## Results

Only 32% of patients were aware of the possibility of developing CRC as a complication in IBD (UC 42%, Crohn's disease – CD 22%, p<0,01). In what concerns the increased risk for CRC in IBD, 68% of patients were aware of it (UC 75%, CD 61%, p<0,01). Very few patients knew that young age at diagnosis and disease duration increase the risk for CRC. Only 29% knew that screening colonoscopies should start 8-10 years after diagnosis. But the best majority of patients (89%) indicated colonoscopy as the standard screening test. Moreover, half of the patients knew that dysplasia is a precancerous lesion. Regarding the therapeutic options, only half of the patients would choose to undergo colectomy in case of dysplasia.

#### Conclusions

This study shows that IBD patients have a low level of education in what concerns CRC as a complication of their disease. Physicians must raise the awareness of IBD patients for a more rigorous disease monitoring and correct therapeutic options in order to reduce CRC prevalence in IBD.

## 7 PREVALENCE AND CLINICAL FEATURES OF PROXIMAL CONSTIPATION IN PATIENTS WITH ULCERATIVE COLITIS

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#### Introduction

Proximal constipation in inflammatory bowel disease is mainly attributable to an accumulation of "feaces" in the right colon, above an area of inflammation. The most common symptoms associated with a slow colonic transit are harder stool consistency, reduced stool frequency, flatulence, cramping, perianal soreness, tenesmus and the feeling of incomplete evacuation. The aim of this study was to assess the prevalence, clinical features and treatment of proximal constipation in patients with ulcerative colitis.

#### Patients and method

We have conducted a clinical retrospective study. 130 patients (male/female: 45/85; mean age: 44.3) with biopsy confirmed UC were included. Symptoms for at least 3 days per month during the previous 3 months were mandatory. Demographic, clinical characteristics and laboratory findings were retrieved from medical records. The variables analyzed were: sex, current age, age at disease onset, disease duration and extent, clinical, endoscopic and histological activity, medication and change in medication.

#### Results

Based on our findings, the prevalence of proximal constipation in UC patients is 44.6% (58 patients). Mean age was 47 years (SD=24.5) and 34 were female. Proximal constipation was associated with left sided colitis (p<0.01) and concurrently active disease (p=0.02). The main symptoms were reduced stool frequency (70.7%), hard, dry stools (56.1%), lower abdominal or rectal pain (48.4%), flatulence (36.1%), anal soreness (27.6%), tenesmus (24.6%) and sensation of incomplete evacuation (16.1%). 85.3% of patients required an increase in rectal doses of 5 ASA and the use of stool bulking agents, osmotic laxatives and dietary fiber supplements (67.9%). There was no significant correlation between proximal constipation and age, disease duration or other changes in therapy.

### Conclusion

Our study demonstrates that proximal constipation is rather common in patients with UC and its risk increases in women with active and distal colon involvement.

## 38 TRENDS IN BIOLOGIC THERAPY AND THEIR IMPACT ON PATIENT QUALITY OF LIFE: RESULTS FROM A PROSPECTIVE COHORT OF ROMANIAN PATIENTS

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# Affiliation: 1- Colentina Clinical Hospital , 2- Carol Davila University of Medicine and Pharmacy

#### Introduction

The introduction of biologics triggered a paradigm shift in treatment options and aims for IBD patients, with the eventual intent of preventing intestinal disability in IBD. Some patients may not be responsive to biologics or lose initial response. This provides incentive to assess biological therapy evolution patterns in IBD patients to understand how to maximize the benefits of biologic therapy.

#### **Patients and methods**

We conducted an interim analysis of a prospective, observational study at a tertiary referral hospital in Romania, including 193 patients with IBD who were prospectively followed with clinical, endoscopic and laboratory data gathered at multiple timepoints. We sought to evaluate biologics initiation trends over the years, effectiveness of early therapy, the rate and reasons for discontinuing biological agents.

### Results

The current analysis included 114 patients, of which 43 patients were on biologic therapy or biologic-exposed. An exponential trend of anti-TNF initiation was observed (R2=1), progressively more diagnosed patients benefiting from biologic therapies (67,5 % biologic naïve at first visit vs 63.1% at follow up-visits). Comparing those treated with IFX versus ADA, there was no difference in discontinuation rates overall (p=0.9) and we found no predictor for therapy cessation (rates of discontinuation are: 19 % for IFX versus 20% for ADA) Higher QoL scores were observed in patients receiving early anti-TNF therapy (initiation within 24 months of diagnosis) when compared to patients receiving late biologic therapy (initiation

 $\geq$  24 months after diagnosis), with median SIBDQ scores 5.8 and 4.8 respectively (p=0.002). Overall, clinical remission rates in biologic exposed patients increased from 39% at first visit to 57% at follow-up (p>0.05) and mucosal healing rates from 13% to 43% (p=0.04).

#### Conclusions

Patients with early anti-TNF initiation have better QoL over time. IFX and ADA withdrawal rates in our cohort are consistent with literature data. More studies evaluating predictors of anti-TNF cessation are needed to discover predictors of response and loss of response in Romanian IBD patients.

# 39 PECULIARITIES OF THERAPEUTIC APPROACH IN CHILDREN WITH IBD

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#### Abstract:

Pediatric-onset IBD (pIBD) requires a particular family-oriented approach, by a dedicated multidisciplinary team, given its unique age-related issues, like negative impact on growth, puberty, nutritional and bone status; increased risk of psychosocial problems; lower adherence to therapy and necessity of a structured transition program to the adulthood healthcare. According to the recent ESPGHAN and ECCO guidelines, deep remission represents the actual goal, as in adult IBD. However, pIBD exhibits a more aggressive phenotype, while less therapeutic options are available and fewer trials involve new drugs. Less colonoscopies are recommended and they could be replaced by fecal calprotectin and, in Crohn's disease (CD) also by imaging techniques (except for computed tomography). In pIBD, the therapeutic approach is selected according to the phenotype and the Pediatric Ulcerative Colitis Activity Score (in UC), respectively the Pediatric CD Activity Index (in CD). More aggressive medical therapy is required, including steroids (with higher rate of steroid-dependency), immunomodulators (IMD) and biologics (both earlier and in higher percentage). Thiopurines and methotrexate are of more benefit in pIBD, respectively in CD. Exclusive liquid diet is more often used in induction of remission in CD, while in pIBD there is less use of rectal 5-aminosalycilates and of long-term combination therapy (biologic and IMD). Surgery is more often required, including resections in CD and colectomies in UC. Side effects should be considered whenever choosing a therapeutic tool, including risk of certain types of malignancy and of intestinal failure, impact on fertility and fecundity, and interference with vaccinations.

### Key words

complications, treatment, safety

# $40 \mbox{Diagnostic yield of small-bowel capsule endoscopy}$ in suspected crohn's disease

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#### Introduction

The role of small bowel capsule endoscopy (SBCE), a relatively

new imaging technique, in investigating Crohn's disease (CD), has expanded with the progresses of the technology, the better understanding of disease pathology and the preference for non-invasive methods. There is no unique, gold-standard diagnostic test for CD, so even if SBCE is the first-line investigation for small-bowel pathology, the diagnosis process implicates both complex clinical judgement and multidisciplinary dedicated approach.

#### **Patients and method**

We retrospectively studied the patients with suspected CD investigated by SBCE in the Institute of Gastroenterology and Hepatology of Iasi, tertiary referral centre, in a two-year period. We analysed criteria for SBCE administration, in terms of clinical, biological and imagistic context, and SBCE diagnostic yield (DY), defined as positive examinations out of total number of patients referred. A specific DY and an overall DY were calculated, respectively. Complications were noted. Follow-up data were studied for assessing predictive value of SBCE.

#### Results

Specific DY of SBCE for suspected CD was 34%. Suspicion index was predictive for CD positive examinations. Overall DY was 73%. Rate of complications was 1.7%. Negative predictive value was high.

#### Conclusion

Even if diagnostic yield of SBCE in suspected CD appears to be below expectations, concomitant elevated overall DY proves global CE usefulness. SBCE is safe and has good general CE performance parameters. Tighter selection could improve specific diagnostic yield. High negative predictive value militates for CE long-term efficacy.

## 41 MANAGEMENT OF LOW BONE MASS IN YOUNG PATIENTS WITH CROHN DISEASE AFTER BISPHOSPHONATES: WHAT`S NEXT?

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## Introduction:

Crohn disease (CD) can be associated with several extraintestinal complications, including bone mass abnormalities. Factors that are linked with it are glucocorticoids, malabsorption, vitamin D insufficiency, chronic inflammation.

We report 2 cases of patients diagnosed with CD:

### Case 1

23-year-old female, diagnosed in 2014, initially managed with ileal resection and subtotal colectomy, at the moment treated with anti TNF, Imuran and prednisolone 24 mg/day, was admitted for back pain.

DXA (dual energy-X ray absorptiometry) revealed BMD L1-L4(L3): 0.883 g/cm2, Z score=-2.4 DS, and the X-ray of the spine showed L2 compression. As she was receiving intravenous bisphosphonates, 43 ibandronate for 2 years, the decision was to initiate teriparatide, a bone anabolic treatment.

#### Case 2

33-year-old, male, diagnosed with CD in 2015, with ileal resection and right hemicolectomy (January 2017); treated with prednisolone 4 mg/day, Imuran 3 tb/day, was admitted for check-up. He had low bone mass density, receiving oral bisphosphonates (risedronat) for 2 years.

The DXA revealed L1-L4 BMD 0.848 g/cm2, Z score=-3,1 DS and left hip=0,678 g/cm2, Z score=-2,6 DS, with partial response to oral

bisphosphonates. The decision for him was also to initiate anabolic therapy, teriparatide, for 24 months.

#### Conclusion

Even if bisphosphonates are used as first-line treatment in glucocorticoid-induced osteoporosis, anabolic effect of treatment with teriparatide can have positive changes on bone mass, in selected cases. Close follow up is recommended to these patients.

# 42 LOW BONE MASS DENSITY IN A PATIENT WITH CROHN DISEASE AFTER 3 MONTHS OF GLUCOCORTICOID THERAPY

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## Introduction

Glucocorticoid-induced osteoporosis is the most common form of secondary osteoporosis in young people. Continuous oral glucocorticoid therapy is associated with rapid bone loss early after the initiation of therapy and it is dose-dependent and correlated to treatment duration.

#### Case report

We report the case of a 48-year-old, male, diagnosed with Crohn disease (CD) in 2017, receiving adalimumab for 7 months, admitted for back pain. He received prednisolone 40 mg/day, decreasing progressively, for 3 months.

He performed a MRI who revealed multiple disc protrusions and a DXA scan showed low bone mass density (BMD), L1-L4: BMD 0.662 g/cm2, T score=-4.3 DS, Z score=-4,5 DS; left hip BMD=0,732 g/cm2, T score=-2,2 DS, Z score=-2 DS. As BMD was low for the short period of glucocorticoids, blood tests were made to exclude other secondary causes. They showed normal kidney and liver function, no anemia, celiac disease excluded, normal gonadal and thyroid function; deficit of vitamin D 19.52 ng/ml, normal PTH level.

The medical management was to correct the vitamin D deficit with colecalciferol 2000 UI/day and to initiate teriparatide, anabolic therapy for 24 months, as he was at increased risk (according ACR guidelines) of developing a fracture.

# Conclusion

Glucocorticoid-induced osteoporosis remains under-treated in the chronic diseases; following initiation of oral glucocorticoids, rapid bone loss happens. Current studies show superiority of teriparatide vs. alendronate for BMD and vertebral fracture outcomes, suggesting using teriparatide as first line option in selected cases.

# QUALITY OF LIFE IN IBD – WHAT IS GOOD ENOUGH?

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#### Introduction

Assessing health-related quality of life (HRQoL) in inflammatory bowel disease (IBD) patients is an ever-expanding practice and, in recent years, HRQoL has proven to a reliable measure of therapeutic efficacy. Our aim was to assess HRQoL and disease activity parameters in a real-life setting and analyze the impact of various therapeutic interventions on HRQoL.

#### Methods

We conducted a retrospective analysis of prospectively collected data from a cohort of IBD patients treated at Colentina Clinical Hospital (the MAID cohort). Patient-reported HRQoL was assessed using the Short Inflammatory Bowel Disease Questionnaire (SIBDQ). The main outcome measure was the change in SIBDQ score over time. To further explore these changes, we administered the SIBDQ to a control-group of healthy voluntaries.

#### Results

Data from 204 patients enrolled in the MAID cohort, totaling of 430 study visits were included in this analysis. Even though the percentage of patients in remission improved over time (36% at first visit vs 56% at second visit), we observed a celling effect of the SIBDQ scores after 24-36 months of follow-up. We observed no significant improvement at follow-up for the SIBDQ scores of patients in clinical remission (median SIBDQ score 5.5 at first visit, 5.7 at second visit, p=0.4, Mann-Whitney U test) vs the scores of the entire cohort (SIBDQ score 4.9 at baseline, 5.4 at second visit, p=0.08)

Surprisingly, lower SIBDQ scores were observed in the control group (67 healthy volunteers, median SIBDQ score 5.2), when compared to SIBDQ scores of patients in clinical remission.

#### Conclusions

Although SIBDQ scores is a useful tool in assessing HRQoL in IBD patients, future studies are required to understand how SIBDQ changes over time can be interpreted and explore whether a ceiling effect truly exists.

## 44 CORRELATION BETWEEN ANEMIA AND CROHN'S DISEASE ACTIVITY: A NATIONAL MULTICENTRIC STUDY BASED ON IBDPROSPECT

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## Background

Anemia is one of the most common extraintestinal manifestation and complication of inflammatory bowel disease (IBD), having multifactorial and complex etiology. The assessment of anemia should be done regularly because of its high prevalence (up to 74%) and impact on the quality of life.

#### Aim

The aim of the study was to evaluate the correlation between the hemoglobin level and the activity and the severity of the disease at patients with Crohn's Disease (CD) in Romania.

#### Materials and methods

The national multicentric registry IBDProspect has gathered up

to 2743 (1135 patients with CD, 1500 with UC, and the rest with nonspecific colitis). Despite the high number of patients registered only a part of the patients had complete data and could be enrolled in the study.

There were analyzed 815 patients with Crohn's Disease in remission or with active disease as defined by the CDAI score (CDAI < 150 remission of CD, CDAI 150-220 mild disease, CDAI 220-450 moderate disease and CDAI > 450 a marker of severe disease). The severity of anemia was evaluated using the WHO anemia grading system.

# Results

The presence of anemia is higher in patients with active disease comparing with the patients in remission (49.42% vs 20.06%, p=0.00001).

Assessing the activity of the disease we discovered anemia in 32.07% of the patients with mild activity. Out of all the patients with moderate activity of the disease, 59.16% of the patients had a degree of anemia. The highest percentage of patients with anemia, 67.56%, was found in the group of patients with severe CD.

## **Conclusion and Discutions**

Anemia has a high prevalence in patients with inflammatory bowel disease, having a great impact on the quality of life of the patients and on the comorbidities. Regarding Crohn's disease, patients in remission had lower anemia rates, while a higher percentage of patients with active disease presented anemia. The prevalence of anemia follows the disease activity, with lower rates in patients with mild disease and higher rates in patients with severe disease activity.

All the patients received the treatment of the disease and of the complication. The patients with iron deficiency with values of Hb<10g/dl received intravenous supplements of iron and the ones with Hb>10g/dl received oral iron supplements.

# 45 EFFICACY OF ADALIMUMAB IN PATIENTS WITH CROHN'S DISEASE WITH LOSS OF RESPONSE TO INFLIXIMAB THERAPY: A SINGLE CENTER RETROSPECTIVE ROMANIAN STUDY

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#### Background

Although Infliximab, a chimeric anti TNF antibody, is effective in inducing and maintaining response in patients with moderate to severe Crohn's Disease, it is known that some patients may experience a loss of response and become symptomatic over time. Adalimumab, a fully human anti TNF antibody, is a well known biologic agent used in the treatment of inflammatory bowel disease. Its efficacy as a second line anti TNF agent in patients with loss of response to Infliximab has been assessed previously in international trials, but local data is lacking.

#### Aims

The aim of this study was to evaluate the efficacy of Adalimumab as second line anti TNF agent in patients with Crohn's Disease who lost response to the Infliximab therapy.

### Material and methods

This is a single center, retrospective study conducted in the Gastroenterology Department of Fundeni Clinical Institute, Bucharest.

There were analised 14 patients with moderate to severe Crohn's Disease as definded by the CDAI score between 220 and 450. All patients have been previously treated with Infliximab and became

# symptomatic over time.

The patients started the Adalimumab therapy following the classical induction protocol 160/80/40mg then 40mg every other week.

The efficacy of Adalimumab as a second line anti TNF agent was analysed after 4 and 12 weeks of treatment, using the CDAI score. The clinical response was characterised by a drop of 70 points in the CDAI score, and the remission by the CDAI score under 150.

## Results

The short term efficacy at 4 weeks of Adalimumab as second line anti TNF agent revealed 7 patients (50%) with clinical response and 3 patients in clinical remission (21,4%). At 12 weeks, 13 out of the 14 patients were still continuing the Adalimumab treatment: 8 patients had a clinical response (57.1% of the entire cohort) and 4 patients were in clinical remission (28,6% of the entire cohort).

## Conclusion

Adalimumab has a proven efficacy as a second line anti TNF agent in the context of Infliximab secondary treatment failure.

The percentage of patients that achieved clinical remission and response is comparable to data from international trials (21% clinical remission and 52% clinical response at 4 weeks in GAIN trial; 32.3% clinical remission and 64.8% clinical response at 12 weeks in ADHERE trial).

Patients continuing the Adalimumab therapy may obtain clinical remission/response over time: 2 patient (14.3%) out of 14 in the study obtained clinical remission or response only after 12 weeks of treatment.

# 46 TNF-ALPHA-308G/A SINGLE NUCLEOTIDE POLYMORPHISM – A NOVEL PREDICTIVE FACTOR FOR THE DEVELOPMENT OF EXTRAINTESTINAL MANIFESTATIONS IN ROMANIAN POPULATION WITH INFLAMMATORY BOWEL DISEASESÂ

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# Introduction

Tumor necrosis factor (TNF) alpha plays a pivotal role in the inflammatory pathways associated with inflamatory bowel diseases (IBD). There are multiple phenotypes of IBD in terms of disease extension, disease severity and association with extraintestinal manifestations (EIM). Treatment molecules have evolved with time, nowadays the interest residing in monoclonal antibodies targeting inflammation molecules like TNF-alpha. Still, approximately one third of patients do not respond to this treatment. Multiple hypothesis have tried to explain this phenomenon some of which have implied genetic differences between individuals.

### Materials and methods

We performed a case-control cross-sectional study to evaluate the role of two single nuleotide polymorphisms (SNPs) in TNF-alpha gene promoter in 92 patients with IBD versus a similar pool of healthy controls. The patients were genotyped for -238G/A(rs361525) and -308G/A(rs1800629) SNPs using TaqMan Allelic Discrimination Assays on a 7300 Real Time PCR System (Applied Biosystems by Thermo Fisher Scientific, USA). Association tests were performed with the software PLINK v 1.07 and p values <0.05 were considered significant.

Results and conclusions

Controls and patients were in Hardy-Weinberg equilibrium for the investigated SNPs. The two SNPs were not significantly different between controls and IBD patients in terms of allele or genotype frequency. We found a significant association between -308A variant and the presence of EIM in both ulcerative colitis and Crohn's disease: p=0.03, OR 6.50 and p=0.005, OR 7.28 respectively. For the whole IBD group -308A allele was more frequent in patients with EIM (26.3%) than in patients without EIM (7.3%, p=0.003, OR 4.5). No other associations with disease phenotype or treatment response were observed.

Based on our results, TNF-alpha -308 SNP can be considered a predictor for extraintestinal manifestations associated to IBD and might be a useful tool for the risk stratification of these patients.

## Key words

inflammatory bowel disease, TNF-alpha polymorphism, SNP

# 47 QUALITY OF LIFE AND ANEMIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN THE IBD PROSPECT DATABASE

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### Introduction

Inflammatory bowel diseases - Crohn's disease and ulcerative colitis – have chronic, wavy evolution and the risk of multiple complications. They are associated with an important consumption of health care resources and have a major impact on the quality of life.

### **Materials And Methods**

The study aims to assess the quality of life in a group of 25 patients with inflammatory bowel disease by applying a questionnaire on diagnostic and treatment, occupational and personal activities in relation to the disease that adversely affects them. Given that one of the most important factors with a negative impact on the quality of life is anemia, we have performed a retrospective multifactorial analysis of patients with anemia from the IBD Prospect database.

## Results

Of the 2191 analyzed patients in IBD Prospect, 43.17% had anemia, of which 55.3% were females and 44.7% males. Depending on the WHO classification system for anemia, 21.7% of all patients with anemia have a mild form, 17.9% a moderate form and 3.6% a severe form. The mean Hb in patients with intestinal inflammatory disease and anemia is 10.2 g / dl. The prevalence of anemia in patients with ulcerative colitis was 39.5%, while patients with Crohn's disease had a prevalence of 41.6%. The risk of anemia is significantly higher in patients with moderately to severe disease and in those diagnosed with intestinal or extraintestinal

# Complications

Differentiation of types of anemia could not be achieved due to lack of data in most patients (ferritin, transferrin, CRP, etc.). Data from the questionnaire shows that patients with severe disease, those with multiple complications and those who underwent surgery have experienced a greater negative impact of the disease on either professional or personal activity and on quality of life in general.

### Conclusions

Anemia is the most common haematological complication of inflammatory bowel disease, being closely related to the degree of activity and the complications of the disease. Combined with the subjective perception of the patients, it significantly lowers the quality of life, and requires regular monitoring, appropriate treatment and psychological support.

# 48 ASSESSMENT OF NUTRITIONAL STATUS IN CORRELATION WITH QUALITY OF LIFE AND DISEASE ACTIVITY IN HOSPITALIZED PATIENTS WITH CROHN'S DISEASE

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## Introduction

Hospitalized patients with Crohn's disease (CD) have an impaired quality of life (QoL) and can develop severe nutritional deficits. SIBDQ is a rapid and reliable measure of QoL and an important patient-reported outcome. Nutritional screening tools (NST) with the most utility in this patients are still unknown.

Aim of this study was to assess the NST which accurately reflect the disease activity and the impact on QoL in hospitalized patients with CD.

#### **Patients And Methods**

The prospective study included 40 patients with CD admitted to our hospital between 2017–2018.

Disease activity was asessed by CDAI score, QoL by SIBDQ and nutritional status by MUST score, NRS2002, O-PNI, CONUT and albumin levels.

Non-parametric statistics were used and correlation was analysed using Spearman rank coefficient (r). Two-sided p<0.005 was considered statistically significant.

#### Results

CDAI was closely correlated with albumin levels (r=-0.74, p<0.005), O-PNI(r=-0.55, p<0.005), NRS2002 (r=0.53, p<0.005) and MUST (r=0.40, p<0.005). An insignificant correlation between CDAI and CONUT was found (r=0.21, p>0.005).

SIBDQ was correlated with albumin(r=0.66, p<0.005), NRS2002(r=-0.58, p<0.005), O-PNI(r=0.51, p<0.005) and MUST(r=0.45, p<0.005). An insignificant correlation between CDAI and CONUT was found(r=0.11, p>0.005).

#### Discussions

These NST have been reported to be useful for predicting prognosis in conditions as chronic kidney disease and chronic heart failure. Malnutrition is common in hospitalized patients with CD and it was easily assesed by these tools. Albumin, O-PNI, NRS2002 and MUST are useful NST and reflect the impact of CD activity and also the impact of the disease on QoL assessed by SIBDQ.

## 49 IBD - ASSOCIATED SPONDYLOARTHROPATY IN THE BIOLOGIC ERA: A CASE SERIES

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#### Introduction

Extraintestinal manifestations (EIM) are frequent and may occur before or after IBD diagnosis, being the proof that IBD is not only limited to gut. The goals of treatment for IBD and IBD-related Spondyloarthropaty (SpA) include reducing the inflammation and preventing any disability or deformity. Here we present a case series of three patients with Crohn's disease (CD) and EIM admitted to our hospital. Patients had in common young age, CD with moderate or severe clinic and endoscopic activity and axial SpA and some particularities: one case associated type 1 peripheral arthritis, another case type II periheral arthritis with enthesitis and oral aphtous ulcers and the last case associated uveitis and erythema nodosum. After failure of conventional therapy with steroids, sulfsalazine or methotrexate, therapy with TNF-inhibitors was initiated (adalimumab) and remission was achieved.

#### Discussions

All cases had in common risk factors for a poor outcome in IBD: disease onset < 40y, the need of steroids or steroid-dependency, deep and extensive colonic ulcerations and the presence of EIM. So, according to literature, these cases presented meet the criteria for "aggressive disease course".

#### Conclusions:

Biologic agents as TNF-inhibitors has changed the therapeutic algorithm and they should be the first line treatment for active IBD and SpA associated. These case reports highlights the importance of TNF inhibitors, this therapy being currently the only effective treatment for patients with aggressive disease or who failed to respond to conventional therapy.

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