OP01. Intensified infliximab induction is associated with decreased colectomy rate in steroid-refractory pediatric ulcerative colitis

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Introduction: Rapid infliximab clearance in patients with severe colitis (Ungar 2016) has led to intensified induction regimens with evidence of greater short-term efficacy in hospitalized steroid-refractory patients (Gibson 2015). Data demonstrating long-term benefit are lacking.

Aims: Patients who received infliximab for steroid-refractory UC at SickKids Hospital, Toronto between June 1, 2003 and July 31, 2015 were retrospectively reviewed.

Material and methods: Induction regimens were prescribed at discretion of treating gastroenterologist, standard being 5mg/kg/dose given at Weeks 0, 2, 6. Intensified induction was defined as mean mg/kg/dose of ≥7mg/kg and/or ≤5 week interval between doses 1 and 3. For all patients, subsequent maintenance regimens (dose/kg and dosing interval) were individualized guided by return of symptoms and, more recently, by infliximab trough levels. Colectomy-free survival was assessed based on standard vs. intensified induction using Cox proportional-hazards models.

Results: The demographic and phenotypic characteristics of the 74 hospitalized patients treated with infliximab for steroid-refractory UC are given in the Table. There were no significant differences between patients treated via intensified (N=37) vs. standard (N=37) induction. 17/74 (23%) patients underwent colectomy over a median duration of follow-up of 12.7 (IQR 5.6-26.2) months. As shown in the Figure, univariable analysis demonstrated a significantly lower colectomy rate for those undergoing intensified induction (HR 0.36, p=0.05). Multivariable modelling demonstrated this significant association was preserved when controlling separately for the effects of age at diagnosis and induction, disease duration, baseline PUCAI, albumin, steroid dosage, BMI z-score, and disease extent. Guided by infliximab trough level monitoring, 18/36 patients were able to decrease mg/kg dose and/or increase dosing interval, usually within the first year.

Conclusions: Intensification of infliximab induction regimen in hospitalized pediatric patients with steroid-refractory UC is associated with sustained reduced risk of colectomy. Dosing and interval between doses can often be de-escalated during maintenance.

OP02. Contribution of individual PCDAI subscores to remission in pediatric patients with Crohn’s disease: results from IMAGINE 1 trial

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Introduction: Pediatric Crohn’s Disease Activity Index (PCDAI) assesses symptoms, laboratory indicators of inflammation, and physical examination results. Previous studies have shown that in patients who responded to treatment, PCDAI subscores of symptoms, albumin, and weight contributed the most to changes in total PCDAI in the short term.1 Aims: To analyze the contribution of individual components of PCDAI to overall PCDAI at baseline and to change in overall PCDAI according to remission status at 4, 26, and 52 weeks.

Material and methods: Patients (N=188) who received adalimumab for up to 52 weeks in IMAGINE 1 were included in the analysis. Patients who prematurely discontinued or escalated to blinded weekly adalimumab were imputed as non-responders (NRI). 2 PCDAI, its subscores, and mean changes from baseline at 4, 26, and 52 were assessed by remission (PCDAI≤10) at respective week and are presented as observed.

Results: PCDAI overall and individual subscores at baseline are shown in Figure. Symptom subscores (abdominal pain, stool frequency, and general well-being) contributed the most to the overall PCDAI at baseline. PCDAI mean change from baseline and contribution of individual subscores’ mean changes from baseline at 4, 26, and 52 weeks by remission status are shown in Table. Symptom subscores represented over 50% and weight and abdomen examination combined represented about 20% of the overall PCDAI change at all time points regardless of remission. ESR contributed more to the PCDAI reduction in patients with remission at 26 and 52 weeks than in those without remission.

Conclusions: Symptom-related subscores represented the majority of the change in PCDAI at baseline, 4, 26, and 52 weeks. Symptoms and abdomen examination subscores contributed to PCDAI decrease regardless of remission status at 4, 26, and 52 weeks.

Whole exome sequencing of over 1000 pediatric IBD patients from a single centre identifies monogenic forms of IBD.

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Background: Inflammatory bowel disease (IBD) has a multifactorial aetiology, with complex interactions between genetic and environmental factors. Recent studies suggest an increasing spectrum of monogenic disease in the very young. The prevalence of these mutations in older children is unknown.

Objectives: To determine the prevalence of monogenic forms of IBD in pediatric patients and identify any phenotypic characteristics allowing for accurate diagnosis.

Methods: 2705 unique participants underwent whole exome sequencing (WES). This data was interrogated for a panel of 51 genes known to be associated with monogenic IBD. The Genome Analysis Toolkit was used to identify highly penetrant rare variants of interest. Sanger sequencing verified variant genotypes. A clinical database was reviewed to ascertain phenotypic characteristics.

Results: A single centre retrospective study identified 1180 index cases, diagnosed over a 13 year period (2003-2015) who underwent WES. 2705 unique participants (556 trios, 31 quads, 34 affected siblings). Of sequenced affected cases, 56% CD, 26% UC, 11% IBD-U, 8% non-IBD. 21% < 6 years, 22% 7-10 years, 57% > 11 years. Across 51 genes, 82 protein coding variants predicted to be deleterious were identified, which were high quality and rare (maf <0.01). Disease causing mutations in XIAP, IL10R, SAP, TTC7A, LRBA, FOXP3, with rare damaging variants in NOX1, XIAP, DKC1 and FOXP3 over-represented in this cohort. Overall, approximately 1% of patients in a typical cohort of Pediatric IBD patients were found to have monogenic disease.

Conclusion: WES of this largest pediatric cohort to date confirms the highly varied phenotypic spectrum of IBD associated with monogenic disease. Most children with causal VEOIBD mutations were diagnosed < 1 year of age, yet a significant number of older children were identified. Characterising genotypic-phenotypic features may provoke earlier recognition which will allow novel therapeutic approaches in this paediatric IBD population.

Keywords: whole exome sequencing, monogenic, pediatric

Cytomegalovirus reactivation complicating pediatric inflammatory bowel disease

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Introduction: Although it has been recommended to perform sigmoidoscopy with biopsies to screen for cytomegalovirus (CMV) reactivation in children with severe, corticosteroid-resistant colitis, the incidence of CMV reactivation and its management in children with inflammatory bowel disease (IBD) is under-reported.

Aim: To determine the frequency and management of CMV reactivation in children with acute severe colitis

Material and Methods: Consecutive patients < 17 years old, with ulcerative colitis (UC), Crohn’s colitis (CC) and IBD-Unclassified (IBD-U) presenting with acute severe colitis and had sigmoid biopsy evaluation for CMV by polymerase chain reaction (PCR) and immunohistochemistry were included.

Results: 91 sigmoid biopsies were collected from 65 patients with endoscopic severe disease: 47 (72.7%) with UC. 8 biopsy samples were obtained from colectomy specimens from patients with UC. 54 (83%) patients had pre-existing IBD, while the rest were newly diagnosed. Medication exposure included corticosteroids for 46 (70%) patients, and immunosuppressive and/or biologic agents for 36 (55%) patients. 27 of 65 patients (41.5 %), were steroid-resistant; 16 with UC, and 11 with CC. The median number of biopsies for CMV PCR per patient was one biopsy (IQR 1 – 2). Four of 47 patients (8.5%) with UC, 2 with steroid resistant disease, had positive biopsies for CMV by PCR but negative CMV serology. They responded to escalated medical therapy, without needing anti-viral therapy, and none required colectomy over a median duration of follow up of 1.1 year (IQR 1 – 1.6). None of those with CC or IBD-U had positive biopsies for CMV.

Conclusions: CMV reactivation may not be common in children with IBD. Studies to examine the underlying sero-prevalence of CMV in pediatric IBD population and its role of reactivation of colitis is required to determine if the current recommendation for routine sigmoidoscopy to exclude CMV infection in corticosteroid-resistant acute severe colitis is justified.

Telemonitoring versus usual care: a multicenter trial among teenagers with inflammatory bowel disease

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Background and objectives: Schedules for follow-up of teenagers with inflammatory bowel disease (IBD) have traditionally been based on providing reassurance, rather than on an estimate of the likelihood of intervening to treat a disease flare. We assessed if a calprotectin-based telemonitoring programme with rapid access to specialist care when need arises could be of benefit for patients with a stable disease course.

Methods: In a prospective multicenter trial we randomly assigned teenagers (10-19 years) with quiescent disease at baseline to the telemonitoring or usual care arm. Teenagers assigned to telemonitoring had biannual checks, and received automated email alerts to fill in a symptom score and to send a stool sample for calprotectin measurement between scheduled visits. Teenagers in the usual care group had regular scheduled visits. After 52 weeks of follow-up we evaluated the cumulative incidence of disease flares per group, defined as increased symptoms necessitating therapy intensification. Secondary outcomes included the quality-of-life score at end of study (assessed with IMPACT-III), cost effectiveness from a societal perspective, and predictors of successful telemonitoring.

Results: We included 170 participants, 84 assigned to telemonitoring and 86 to usual care. After 52 weeks of follow-up, the percentages of patients with a disease flare were similar in both arms (respectively 33% and 34%). The quality-of-life score at the end of the study favoured the telemonitoring arm (79 vs 75, P=0.02).

Telemonitoring saved €360 per patient annually, provided that patients responded to at least 80% of the automated alerts. A higher emotional quotient and living further away from the hospital were predictors of better compliance to the telemonitoring programme.
Conclusions: Calprotectin-assisted telemonitoring of teenagers with IBD seems as effective and safe as traditional care. Better disease specific quality-of-life and lower costs make this telemedicine solution the preferred strategy for monitoring teenagers with a stable disease course.

**OP06. Childhood-onset inflammatory bowel disease and subsequent school performance – a population based cohort study**

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Introduction and aims To test the hypothesis that childhood-onset inflammatory bowel disease (IBD) has a negative influence on school performance and is a risk factor for compulsory school failure.

Material and methods Cohort study in nation-wide registers with prospectively recorded information. We identified 2,827 children with IBD (CD: n=1207; UC: n=1370; IBD-U: n=250) through hospital-based inpatient and outpatient data in the Swedish Patient Registry 1990-2013. Index patients were matched with up to ten reference individuals for age, sex, year and place of residence (n=28,235). First-degree relatives were identified through the Multigeneration register and in restricted analyses we compared siblings only with each other. Data on school performance and educational achievement were obtained through the National School Register. Linear and logistic regression models controlling for socioeconomic factors were used to analyze school performance as grade point averages (maximum 320 points) and the risk of school failure (finished compulsory school without qualification for high school).

Results Children with IBD had significantly lower grade point average (adjusted mean difference -4.9 (95% CI -7.1 to -2.6)) and an increased (but not significant) risk of school failure (OR 1.14 (95% CI=0.99-1.31). Underperformance was more common in children with a severe disease course (long duration of active disease and need for inpatient treatment and intra-abdominal surgery). When restricting the analyses to siblings, the association of IBD with lower grade point average remained (adjusted mean difference -6.2 (95% CI -8.7 to -3.7).

Conclusions: Overall, childhood-onset IBD seem to have a modest negative effect on compulsory school performance. However, the more frequent underperformance of children with long standing active disease implies that this subgroup should be identified early and continuously be provided extra school support to minimize the negative impact of chronic disease.

**OP07. Patient engagement in research: using the james lind alliance process to identify the top 10 research questions in pediatric IBD**

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Background: There is increasing emphasis among clinicians and funders on patient-centered care. This study sought to identify the most important unanswered questions about pediatric inflammatory bowel disease (IBD) from the perspective of pediatric patients, their caregivers, and the health care professionals who care for these patients.

Methods: The priority setting methodology, developed by the James Lind Alliance, involved four key stages: gathering research questions; checking these against existing evidence; interim prioritization; and a final consensus meeting during which the top ten unanswered research questions were agreed using modified nominal group methodology. The research was led by a national steering committee composed of clinicians, patients and parents of children with IBD. Research uncertainties were identified through an online Canadian survey of pediatric IBD patients, their caregivers, and health care professionals.

Results: 366 participants completed an online survey, eliciting 1209 raw questions. Once similar questions were combined, 626 unique questions were identified. These were reduced to 388 after eliminating out of scope and already answered questions (according to the literature and content experts), and through a qualitative analysis delineated into 17 themes. From this list, 78 indicative questions were derived by the steering committee, together with 32 questions from clinical practice guidelines. After an online, national vote, a list of the 30 most highly ranked questions were tabulated. This list was further reduced to 19 questions and discussed at a priority setting workshop reaching consensus on the top 10. This final list included questions about the causes of IBD, the role of diet in the management of IBD and the role of novel biomarkers in assessment of disease.

Conclusions: Through meaningful engagement of patients, caregivers and clinicians we have identified their research priorities, which will be used to guide researchers in designing future studies and inform health care funders.
OP008. Transcriptional Analysis of Intestinal Epithelial Organoid Cultures Derived from Pediatric Crohn’s Disease Patients

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Crohn’s disease (CD) is a chronic inflammatory disorder of the intestine with onset occurring from childhood to late age. Growing evidence reveals the importance of epithelial barrier changes in the perpetuation of CD. We hypothesize that patient age can predispose the intestinal epithelium to the acquisition of specific expression alterations. In order to demonstrate this, we investigated the transcriptional signature of intestinal epithelial organoid cultures (EpOCs) derived from pediatric and adult patients with CD.

Biopsy samples from the ileum and colon of pediatric and adult patients with CD were collected. Isolated crypt units were used to generate EpOCs. After ex vivo expansion, EpOCs were induced to differentiate into the main intestinal epithelial lineages (d-EpOCs), and total RNA was extracted for expression profiling. Pediatric and adult EpOCs followed similar differentiation programs when induced to generate d-EpOCs, while maintaining a colon versus ileum-specific pattern of marker expression. Nonetheless, a panel of genes was significantly altered in colonic EpOCs generated from pediatric versus adult CD patients. Several of these genes were associated with the induction of a pro-inflammatory response (i.e., CXCL gene family, REG1A, RETNLB).

EpOCs are promising ex vivo system to explore the presence of changes imprinted in the intestinal epithelium of CD patients. Our results suggest that pediatric CD patients harbor specific lasting alterations in the epithelial compartment. This could contribute to differently shaping the phenotype of the disease in these subjects.

Keywords: pediatric CD, intestinal epithelium, EpOCs, expression profile, lasting alterations

OP009. Stromal Cell – Innate Immune Cell Interactions in Pediatric Inflammatory Bowel Disease Patients

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Background and objectives: The importance of stromal-immune cell interactions in the persistence of chronic inflammation is rapidly emerging. We have recently discovered that, in newly diagnosed and treatment naïve pediatric inflammatory bowel disease (IBD) patients, a certain subpopulation of neutrophils represents the main source of a key regulatory cytokine, interleukin (IL)-23 (Gut, 2016). The main objective of our work is to identify the essential stromal-immune cell crosstalk components that would be targetable in the clinic.

Methods: Blood and intestinal biopsies from newly diagnosed and treatment naïve as well as established pediatric IBD patients were analyzed using confocal microscopy, flow cytometry, cell sorting and CLARITY, a method that makes tissue transparent.

Results: Confocal microscopy analysis revealed that fibroblasts in subepithelial regions in IBD patients, but not the controls, were positive for Podoplanin - a glycoprotein that plays crucial roles in immune cell biology in health and disease. In addition, the subepithelial colonic fibroblasts were STAT3 positive. Interestingly, using flow cytometry we identified IL-22R+Podoplanin+ fibroblasts in active IBD, but not in the controls – nor the IBD patients in remission. Moreover, we performed 7-color confocal microscopy in order to define spatial distribution of fibroblast subpopulations of interest in relation to neutrophils and macrophages, as well as CLARITY to perform a 3D visualization of Podoplanin+ fibroblasts in human colon.

Conclusions: Our recent yet unpublished data support the hypothesis that neutrophils may act on intestinal fibroblasts via IL-23/IL-22 and STAT3 signaling, leading to alterations in the stromal cell niche. Along with unique immune-stromal cell spatial insights in human gut architecture, our work contributes to a better understanding of the stromal cell – innate immune crosstalk in pediatric IBD patients and provides a platform for translational research that we believe will lead to better diagnostics, monitoring and treatment of pediatric patients with IBD.

OP10. Development and validation of the “mini index” (mucosal inflammation non-invasively index) for crohn’s disease on a large prospective pediatric cohort

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Background: Mucosal healing (MH) has become an important therapeutic goal in Crohn’s disease (CD). Repeated assessments by ileocolonoscopy are less feasible, especially in children. The Pediatric Crohn’s Disease Activity Index (PCDAI) does not correlate well with mucosal inflammation. We aimed to develop and validate a multi-item index, based on clinical and laboratory parameters, which could reflect MH in clinical trials as well as for clinical practice, termed the MINI-index (i.e. Mucosal-Infammation, Non-Invasive).

Method: This study utilized data from the large prospective ImageKids study where children with CD underwent ileocolonoscopy concurrent with recording of explicit clinical and laboratory data, including calprotectin, at disease onset or thereafter. PCDAI items, laboratory tests and FC, were associated with the Simple Endoscopic
OP11. Efficacy of Vedolizumab in Anti-TNF refractory Pediatric Ulcerative Colitis: Data from the Canadian Children Inflammatory bowel disease Network (CIDsCaNN).

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Background: Whilst anti-TNF antibodies are highly effective in treating paediatric IBD, a proportion of patients fail to achieve adequate response, experience intolerance and/or become unresponsive over time. An alternate pathway biologic has been particularly needed in UC, where primary non-response to anti-TNF is more common.

Aim: We aimed to assess the efficacy and safety of Vedolizumab in paediatric patients with anti-TNF refractory Ulcerative Colitis.

Methods: In January 2016 Vedolizumab was approved in Canada for children with IBD who had failed anti-TNF. Eligible patients at SickKids Hospital and within the CIDsCaNN inception cohort at other sites had clinical and biochemical data prospectively recorded at each infusion. Clinical response was assessed using PUCAI at week 10 and 6 months. Endoscopic response was assessed centrally via Mayo-ES of colonscopies performed >/= 6 months following first infusion. Results: 35 eligible UC/IBD-U patients commenced Vedolizumab (55% female; median age 15.2 (range 5-17)). 8 had coexisting PSC. 81% were receiving corticosteroids at baseline. At week 10, 76% patients had response (PUCAI decrease >/=20) and 48% clinical remission (PUCAI <10). 44% of patients were steroid-free. In patients with elevated baseline CRP, 25% had normalised CRP at week 10. At 6 months, 55% of patients had achieved clinical remission. In patients with follow up endoscopy, 70% had an endoscopic response (Mayo ES decrease >/= 1); only 1 achieved complete mucosal healing (Mayo ES 0). In patients with PSC, 63% of patients were in steroid free clinical remission at week 10. One patient developed pneumonia requiring hospitalisation.

Conclusion: These data support the use of Vedolizumab in paediatric patients with anti-TNF refractory UC/IBD-U. Outcomes in PSC-IBD are also encouraging.

ORAL NURSES AND DIETITIANS’ PRESENTATION

NPOP01. Outcomes from patient pre visit planning (PVP) in Pediatric Inflammatory Bowel Disease (PIBD) using the ImproveCareNow (ICN) tool.

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Introduction and aims: ICN is a quality improvement collaboration of 96 PIBD international centres. An important concept of ICN is PVP for clinics, recently PVP for patients and parents prior to their next clinic appointment, as patient reported perception is important to holistic care. Concerns of patients must be considered when discussing care plans and promoting good quality care. Our aim was to PVP the concerns of patients at our center before their appointment.

Material and Method: For each patient attending clinic we request they fill in a self reported clinical activity score. Additionally we ask them to report their biggest concern before clinic. We retrospectively reviewed these over a 6 month period.

Results: 60 patients attended clinics, females n=32, age range 4-18 years mean average 8.9 years. 30/60 had Crohn’s disease, 21 had IBDU, 5 UC and 2 had EoIBD. 36 had no concerns, 24 raised concerns. Themes were concerns related to their IBD flares n=5 blood in stool n=2, abdominal pain n=2, abdominal pain n=1,
Others n=2 (weight loss and poor appetite), medication questions n=4. 30 patients that reported no concerns also had matching quiescent disease in our subjective global assessment (SGA). In contrast to this 12 patients with quiescent SGA still reported concerns about their IBD themes included medication queries n=3, day to day activities n=1, growth concerns n=2.

Conclusion: Our review highlights the importance of PVP for patients before their appointment to help reduce patient anxieties therefore improving quality of life. In future adding psychological screening tools would also increase the possibility of identifying patients that may need further psychological support.

NPOP02. Qualitative study of children, adolescents and parents ’ perspective after recent diagnosis with inflammatory bowel disease

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Introduction: A diagnosis of a chronic illness is a life-altering experience for a child and family. Specifically, the first couple months of diagnosis may be overwhelming as the family struggles to manage the disease while aiming to continue on with responsibilities of daily life. The purpose of this study was to elicit children and parent perspectives following a diagnosis of Inflammatory Bowel Disease (IBD).

Material and Methods: A qualitative description design was employed. Seventeen patients were recruited from a Pediatric IBD Clinic in Western Canada. Interview was employed to gather perceptions, opinions, and attitudes from patients and their parents. Transcriptions of the interviews were analyzed using a qualitative content analysis.

Results: Four themes were identified: perspective of diagnosis, roles in care and decision-making, sharing the diagnosis, and treating the disease. Children and parents expressed varied emotions in response to diagnosis. Families articulated the desire to become more active members in the decision-making process with regards to what treatment was chosen. While using conventional medical therapy was seen as an appropriate choice for short-term therapy to get the disease into remission, many parents hoped that more conventional and alternative therapies could be used in the future once the disease was brought into remission.

Conclusion: Healthcare providers need to provide excellent education on the disease process, treatment options, and the use of complementary and alternative medical therapy in IBD, while at the same time supporting children and parent’s voices in treatment decisions.

NPOP03. The development of a nurse-led inflammatory bowel disease outpatient clinic: Meeting the needs of adolescents with inflammatory bowel disease

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Background: Given the incidence of adolescents’ inflammatory bowel disease (AIBD) is increasing, it is important that the services provided to care for these patients meet their needs. With the development of IBD nurse-led clinics at our centre, the IBD nursing team aimed to understand the views and needs of their adolescent patients in order to help establish these clinics, whilst ensuring that the service is tailored to their needs.

Method: A qualitative service evaluation study was conducted through semi-structured interviews with 7 adolescent patients users, four of the participants were male and three were female. Participants were asked six open ended questions on the IBD nursing service they currently receive, their opinions on what they wanted to be included on the IBD nurse-led clinic and their thoughts and ideas on attending a shared medical appointment (SMA) with other adolescents with IBD.

Results: Data was analysed using thematic analysis. The study showed a general lack of knowledge regarding IBD, treatment involved and disease progressions. Adolescents felt that interaction with healthcare professionals (HCPs) was limited with most discussions around their disease being facilitated by their parents. The adolescents showed a desire for support from HCPs and their peers with IBD. Their knowledge of services available was limited, barriers contributing to this included their age, lack of knowledge of IBD and prominent parental involvement. There was a concern with confidentiality with SMAs, but most adolescents would attend.

Conclusion: Our service evaluation study in these AIBD patients identified four themes: the general lack of knowledge; interactions with HCP; lack of knowledge of services; and support needs. This supports the establishment of nurse-led AIBD outpatient clinics to facilitate the identified themes. It is hoped that SMA without parental involvement will help gap educational needs and facilitate peer support.

Key words: Adolescent; Nurse-led clinic; Shared medical appointments

NPOP04. Use of Exclusive Enteral Nutrition in Pediatric Crohn’s Disease in the Indian subcontinent

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Background: The use of Exclusive Enteral Nutrition (EEN) for management of Crohn’s disease (CD) is a well-established and evidence based treatment. There are no pediatric studies in the Indian sub-continent which have been published till date.

Aim: To assess the outcome of EEN in pediatric Crohn’s disease in inducing remission.

Method: A prospective, observational study over a 5 year period was done in a tertiary level children’s hospital. The cohorts were assessed nutritionally and their disease activity measured using Patricide Crohn’s disease activity Index (PCDAI). EEN was recommended for a period of 6-8 weeks. Achievement of disease remission was measured by outcomes such as PCDAI and increase in weight at the completion of EEN therapy.

Results: A total of 30 children, 20 males and 10 females were included. Prior to the therapy, 36.66 % were well nourished, 60 % were underweight and 3.33 % were obese. 29 children gained weight during the course of EEN, with mean gain of 4.00 ± 1.75 kg. In the overweight child, 2 Kg weight loss was noted. At the end of the therapy, 90 % of children were well nourished.28 children were well into remission at the end of EEN therapy.
PCDAI differences were seen in all patients and an improvement was noted. During the entire course of treatment, no side effects were noted due to EEN. In patients who achieved complete remission, weight for height and Body Mass Index for age improved significantly between the commencement and end of treatment with EEN. There was significant (p< 0.05*) weight gain at the end of therapy.

Conclusion: Use of EEN is an effective treatment in achieving remission of active pediatric CD, with no associated systemic side effects when compared to corticosteroid therapy.

Key word: Exclusive Enteral Nutrition, Pediatric Crohn’s disease.

E-POSTERS

EP01. Shotgun Metagenomics, 16S rRNA Gene Sequencing, and Human Genetics Differentially Classify Pediatric Crohn’s Disease State and Treatment Outcome

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Background and objectives The microbiome in Crohn’s disease (CD) differs between mucosal and stool samples, with biopsies arguably reflecting disease pathogenesis better. Microbiome analyses of CD biopsies have been cost-limited to 16S rRNA gene (16S) profiling. We performed the first metagenomic sequencing (MGS) of biopsy samples in treatment-naive paediatric CD. Our aim was to integrate MGS, 16S and whole human genome data.

Methods Colonic biopsies of 20 CD and 20 normal colon controls were sequenced for MGS and 16S. Human genome data for 133 known CD risk loci allowed calculation of genetic risk score (GRS). MGS and 16S-based analyses were used to call taxa at strain level and identify functional profiles.

We investigated how these datasets classified CD disease state and predicted treatment response using a predictive modelling program to determine accuracy in predicting CD risk. We classified CD patients as responders and non-responders to induction treatments, started at the time of diagnosis.

Results Each 16S taxonomic dataset classified patients by disease state with high accuracy (maximum 84.2%), as could GRS, however no MGS taxonomic dataset could significantly classify patients by disease state (Figure 1A). The two most informative 16S genera were Desulfovibrio and Akkermansia. After classifying CD patients based on their response to induction treatment response, 16S genera were again the top dataset, but MGS datasets were also significant classifiers (Figure 1B).

Conclusions Taxonomic profiles from 16S and GRS accurately differentiate disease from control samples, though MGS data cannot. Both the 16S and MGS datasets can however be used to identify differences in microbial taxa with respect to predicting remission from induction therapy in paediatric CD. 16S datasets are cost-effective and probably adequate for most purposes, but are complemented by MGS for detailed clinical interrogation.

Keywords Crohn’s disease; microbiome; metagenome; genetic risk score; treatment response

![Figure 1: Classification accuracies for all datasets classifying A) disease state and B) treatment response. The symbols *, **, and *** indicate significance at P < 0.05, P < 0.01, and P < 0.001, respectively.]

EP02. Characterization of the T cell Receptor Repertoire in Pediatric Ulcerative Colitis

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Introduction: T cells have an important role in the pathogenesis of IBD. The antigenic specificity of these cells occurs via generation and rearrangement of a functional T cell receptor (TCR). High throughput sequencing (HTS) permits detailed assessment of TCR repertoire patterns. There is limited data whether TCR repertoires are altered in IBD patients. We hypothesized that pediatric UC patients possess unique TCR repertoires resulting from clonotypic expansions in the inflamed tissue.

Aim: To characterize TCR repertoire patterns in pediatric UC patients.

Materials and Methods: DNA was isolated from blood and rectal biopsies of newly-diagnosed pediatric UC patients and healthy controls. HTS was performed to determine the TCRβ repertoire. Such a strategy, which employs massive parallel sequencing to process millions of rearranged TCR products simultaneously, permits an in-depth analysis of individual TCRs at a nucleotide level.

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Results: Paired blood and rectal biopsies were collected from 4 control subjects and 8 UC patients (3 with severe disease). In both patients and controls, the TCR repertoire was more clonal in the intestine, compared to the blood, and was further restricted in those patients with acute severe colitis. In several patients, specific clones were highly upregulated in the blood or rectum, each one representing more than 5% of the total repertoire. Shared clones between blood and rectum in each subject were significantly higher among patients vs. controls. However, despite a similar clinical phenotype, the frequency of shared clones between patients was extremely low. Finally, in a patient with limited proctosigmoiditis, numerous clones were shared between the distal inflamed and proximal non-infamed colonic tissue.

Conclusions: HTS of the TCR is a powerful tool for studying adaptive immune cell function in the gut. The oligoclonality observed among UC patients suggests specialization of unique T cell clones, that likely have a role in mediating tissue damage.

EP03. Age-of-Onset Dependent Ileal Immune Maturation and Reduced Alpha-Defensin Expression in Pediatric Crohn’s Disease despite Stable Dysbiosis


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Introduction: Variation in disease location and antimicrobial sero-reactivity across age-of-onset has suggested fundamental differences in pediatric Crohn Disease (CD) pathogenesis. While this could include the spatiotemporal relationship around puberty that a peak incidence of ileal involvement and Peyer’s patches maturation, represented by IFNγ-expressing Th1 cells, direct mucosal evidence was lacking. We aimed to characterize differences in the ileal global pattern of gene expression and microbial community in treatment-naive pediatric CD patients in older (A1b ≥10 years) compared to younger (A1a <10 years) patients. Material and methods: Here we characterize the ileal global pattern of gene expression using RNA sequencing and microbial community using 16S DNA sequencing in 304 treatment-naive pediatric CD patients and non-IBD controls (Ctl) enrolled at 28 North American sites. Results: We show a robust ileal gene signature notable for higher expression of specific immune genes including GM-CSF and IFNy, and reduced expression of antimicrobial Paneth cell derived α-defensins, in older (A1b ≥10 years) compared to younger (A1a <10 years) patients. Reduced α-defensin expression in older patients was associated with higher IFNy expression, but largely independent of NOD2 or ATG16L1 risk allele carriage. By comparison, the CD-associated ileal dysbiosis, characterized by expansion of Enterobacteriaceae and contraction of Bacteroidales and Clostridiales, was already established within the A1a group and did not vary with increasing age-of-onset. Conclusions: These data provide evidence for maturation of mucosal Th1 immune responses and loss of epithelial antimicrobial α-defensins with increasing age-of-onset in pediatric CD despite the observed stable dysbiosis across all ages of onset. These specific host factors and microbial composition offer the potential to tailor future age-based therapy.

EP04. Variability of core microbiota in newly diagnosed treatment-naive Pediatric Inflammatory Bowel Disease patients

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INTRODUCTION Intestinal microbiota is considered to play a crucial role in the aetiology of inflammatory bowel disease (IBD). Insight in the dynamics of the microbial ecosystem in IBD patients is currently limited.

AIMS To describe faecal microbiota composition and dynamics in a large cohort of children with de novo IBD, in comparison to healthy controls (HC).

MATERIAL AND METHODS In this prospective study, performed at two tertiary centres, faecal samples from newly diagnosed, treatment-naive paediatric IBD patients were collected prior to bowel cleansing for colonoscopy (t0) and after 1, 3 and 6 weeks and 3 months. Disease activity was assessed by global physician assessment (GPA) score, faecal calprotectin and C-reactive protein levels. Microbiota analyses were performed by 16S-pro. Microbiota composition was analysed by principal coordinate analysis (PCoA) and Shannon diversity index. Overall differential bacterial expression profiles were assessed by a global test. Group-regularised logistic regression was used to assess bacterial classification signatures. Predictive performance was evaluated by receiver operating characteristic (ROC) curves.

RESULTS Microbial profiles of 104 new IBD-patients (63 CD, 41 UC, median age 14.0 years) were compared to 61 HC (median 8.8 years). IBD was mainly characterised by decreased abundance of Alistipes finegoldii and Alistipes putredinis, which characterize a healthy state microbial core. The classifier including these core species as predictors achieved an AUC of the ROC curve of .87. Core bacteria tended to regain abundance during treatment, but did not reach healthy levels.

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CONCLUSIONS Faecal microbiota profiles of children with de novo CD and UC can be discriminated from HC with high accuracy, mainly driven by a decreased abundance of species shaping the microbial core in the healthy state. Paediatric IBD can therefore be characterized by decreased abundance of certain bacterial species reflecting the healthy state rather than by the introduction of pathogens.

EP05. Histopathological quantitative analysis of cd30+ lymphocytes in bowel mucosa can improve differential diagnosis of pediatric Crohn’s disease and ulcerative colitis

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Background and objectives The histopathological discrimination of Crohn’s disease (CD) and ulcerative colitis (UC) can be a difficult task, especially in pediatric cases. The aim of this study was to find out, whether the microbiological quantification of CD30+ lymphocytes in bowel mucosa can improve the accuracy of diagnosis of pediatric inflammatory bowel disease (IBD).

Methods We performed a retrospective study on 60 pediatric patients with IBD (30 with CD and 30 with UC). Biopical samples from six different regions (terminal ileum, caecum, colon ascendens, transversum, descendens and rectum), taken during the first endoscopy at the time of diagnosis, were stained with anti-CD30 antibody and number of positive cells per one high power field (HPF) were calculated.

Results We found a significant difference between the medians, mean values and maximal numbers of CD30 positive cells in CD and UC (p<.001 for all values). A differences between the numbers of positive cells in separate bowel segments were also recorded, highest in rectum (p<.001). The cut-off value for rectal biopsies, determined by the receiver operating characteristic curve, was 5 cells/HPF, which had a sensitivity of 75% and specificity of 97% for the diagnosis of UC.

Conclusions Immunohistochemical quantification of CD30+ lymphocytes can discriminate pediatric CD and UC with a high sensitivity and specificity, especially in rectal region.

Keywords: inflammatory bowel disease; immunohistochemistry; CD30

EP06. Use of IgG-binding as a marker of bacterial virulence in the terminal ileum of pediatric IBD patients

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Introduction: Several studies support a role for gut microorganisms in the development of Crohn disease (CD) and ulcerative colitis (UC); however, most research has examined samples from stool or inflamed areas, limiting the ability to differentiate between cause and effect. We have shown changes in diversity and composition of bacteria from the uninfamed terminal ileum (TI) in pediatric UC, suggesting that microbes proximal to diseased areas may drive inflammation distally. In an effort to identify these microbes (pathobionts), and as we hypothesized that immunoglobulin (Ig)G is formed in response to invasive microbes, we aimed to isolate IgG-bound bacteria and test their potential virulence in-vitro.

Methods: Luminal washes were collected from the TI of pediatric IBD patients and non-IBD controls during endoscopy. IgG-bound (IgG+) and unbound (IgG-) bacteria were collected using fluorescence-activated cell sorting. DNA was extracted and analyzed by 16S sequencing using the Illumina MiSeq platform and the virulence of specific IgG-bound bacteria was tested in-vitro.

Results: Species diversity was reduced and microbial composition altered in UC compared to non-IBD. Furthermore, the ratio of IgG+/IgG- bacteria was increased in CD and UC patients by 2- and 1.5-fold, respectively. Although total abundance of Burkholderia cepacia, previously identified in the ileum of IBD cohorts, was comparable in IBD and non-IBD, there was a 2.5- and 4.1-fold increase in the ratio of IgG+/IgG- binding to B. cepacia in remission/mild or moderate/severe UC, respectively, compared to non-IBD. B. cepacia displayed pro-inflammatory effects and invasive potential in an in-vitro model, supporting its pathobiont potential.

Conclusion: We have demonstrated the ability of IgG-binding to selectively identify previously unrecognized mucosa-associated pathobionts, validated in-vitro. Elucidating the role of specific bacterial species in UC pathogenesis will underpin new strategies to improve our ability to direct therapies to those patients most likely to respond.

Keywords: microbiota, pathogenesis, IgG, mucus penetration

EP07. Innate Lymphoid Cells in Pediatric Inflammatory Bowel Disease

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Background and objectives: The incidence of paediatric IBD (PIBD) is on the rise. However, the underlying etiology of PIBD remains largely unknown, indicating the dire need for more knowledge on the mechanisms operating this disease. Innate lymphoid cells (ILCs) constitute an important component of the mucosal immune system. Recent years have seen an increase in ILC knowledge, with numerous publications highlighting the importance of ILCs in murine and adult IBD development and progression. In this project, we aim to elucidate the role of ILCs in the development and disease severity of PIBD.

Methods: ILCs were isolated from colon biopsies and peripheral blood mononuclear cells (PBMCs) of paediatric patients admitted to the Paediatric Gastroenterology Unit at the Department of Women’s and Children’s Health, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden. ILC population frequencies and phenotype were examined by 18-colour flow cytometry and correlated to children’s IBD physician global assessment (PGA) scores.
Results: Preliminary results from 11 PIBD and 5 non-PIBD patients show that the frequencies of ILC1 and NKp44-negative ILC3 cells in the gut are increased in paediatric IBD as compared with non-PIBD control patients (p ≤ 0.01, * for both). As well as this, the frequency of colonic CD56dim NK cells directly correlated with the PGA score (p ≤ 0.03, *).

Conclusions: Our initial data suggests a correlation between ILC population frequencies and PGA disease scores in PIBD. Further research must be conducted to examine additional phenotypical and functional differences in ILCs from healthy as compared with IBD patients.

Keywords: innate lymphoid cells, paediatric, inflammatory bowel disease.

EP09. Correlation between gut environment and bacterial invasion in pediatric inflammatory bowel diseases
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Background and objectives: A balanced host–microbial relationship, which orchestrates gut homeostasis and immune regulation, is disrupted in inflammatory bowel diseases (IBD). We hypothesized that an altered gut luminal environment in IBD can impact the virulence capacity of bacteria, leading to disruption in homeostasis and disease. We aimed to investigate the relationship between microbial virulence and gut microenvironment.

Methods: Intestinal aspirates were collected during endoscopy from 10 non-IBD controls, 9 Crohn Disease (CD), and 10 ulcerative colitis (UC) pediatric patients. In vitro invasion of bacteria isolated from the duodenum and terminal ileum (TI) was quantified using gentamicin protection assays. Known Escherichia coli strains were inoculated with patient intestinal aspirates and epithelial cells in vitro to assess the effects of the gut microenvironment on bacterial invasion. Metabolomic NMR analysis was conducted on intestinal aspirates to identify factors that could explain the observed effects, which were then confirmed in vitro.

Results: There was no difference amongst the in vitro invasion potential of bacteria obtained from the intestinal aspirates of non-IBD and IBD patients. Incubation of E. coli strains with intestinal aspirates from IBD patients, but not non-IBD, significantly altered their in vitro epithelial invasion. NMR metabolomic analysis of aspirates revealed metabolites that correlated with bacterial invasion; succinate present in the intestinal aspirates correlated positively, while acetate and formate related negatively with invasion. Addition of exogenous succinate increased invasion of E. coli in vitro.

Conclusions: Our results indicate that alterations in the gut microenvironment in IBD can affect bacterial invasion. Succinate is associated with increased bacterial invasion and can alter bacterial virulence in IBD, while acetate and formate related to decreased virulence. This study highlights the interaction between specific metabolites and bacteria that could be instrumental in propagating or suppressing inflammation in pediatric IBD patients.

Key words: IBD, metabolomics, inflammation.

EP10. Severe Lymphomnodular hyperplasia and IBD-like Phenotype due to an Activating PIK3CD Mutation
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Background: Numerous rare mutations in genes implicated in immune function have been identified in recent years as causing very early-onset IBD (VEO-IBD) in some patients. Activated phosphoinositide 3-kinase δ syndrome (APDS) is a recently described primary immunodeficiency resulting from PIK3CD mutations that lead to recurrent infections.

Aim: To characterize the gastrointestinal manifestations of patients with APDS who presented with a severe IBD-like phenotype.

Materials and Methods: Detailed immune work-up was performed in three patients who presented with very early-onset IBD. Whole exome sequencing was used to identify pathogenic variants. In a single patient and two healthy controls Mass CyTOF on blood and intestinal immune cells provided deep immune phenotyping.

Results: All patients developed recurrent sinopulmonary infections, bronchiectasis and splenomegaly. In addition, the patients presented in the first years of life with chronic diarrhea and failure to thrive due to severe intestinal lymphonodular hyperplasia and an IBD-like phenotype. Two of the patients developed colonic diffuse large B cell lymphoma in adulthood. Immune work-up displayed T cell lymphopenia in all patients and dysgammaglobulinemia in two of them with marked elevation of IgM. Whole exome sequencing in all patients revealed a dominant de-novo activating mutation (E1025G) in PIK3CD gene encoding the catalytic subunit of phosphoinositide 3-kinase δ. Mass CyTOF analysis showed a marked decrease in B cells in the intestine and blood in one of the patients vs. controls, accompanied by an increase in memory CD4 and CD8 cells. Moreover, patient’s circulating CD4 and CD8 T cells produced very high quantities of IFNγ and TNFα.

Conclusions: Gain-of-function mutations in PIK3CD should be included in the differential diagnosis of VEO-IBD. Severe intestinal lymphonodular hyperplasia in early childhood should alert physicians of APDS. Novel PI3K inhibitors currently studied as anti-cancer agents should be evaluated as a potential targeted therapeutic modality in patients with APDS.

EP11. Very–Early-Onset Inflammatory Bowel Disease (VEOIBD); clinical presentation, response to therapy and prognosis.

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The term Very Early Onset IBD (VEOIBD), describes intestinal inflammation presenting in children younger than 6 years. It usually presents with extensive disease, greater colonic involvement, and aggressive clinical course. Our objective is to describe our VEOIBD patients.

Methods: We included all VEOIBD patients diagnosed in our centre (2002-2016). Baseline characteristics, clinical parameters, treatment and long-term evolution were collected.

Results: 24 patients (15 boys) were included. Mean age at diagnosis, 33 months (range: 8-64m). The most frequent symptoms at presentation were diarrhoea (100%), rectal bleeding (95%), abdominal pain (54%) and weight loss (54%). Mean time of diagnostic delay 5.5 months (1-18m). Anaemia was present in 58%, increased ESR and/or CRP in 41% and hypoalbuminemia in 12.5%. Pancolonic involvement was the most frequent finding. Eighteen patients (75%) showed a pattern suggestive of UC, 3 of CD and 3 were classified as IBDU. Severity at onset was moderate in 64m. The most frequent symptoms at presentation were diarrhoea (100%), rectal bleeding (95%), abdominal pain (54%) and weight loss (54%). Mean time of diagnostic delay 5.5 months (1-18m). Anaemia was present in 58%, increased ESR and/or CRP in 41% and hypoalbuminemia in 12.5%. Pancolonic involvement was the most frequent finding. Eighteen patients (75%) showed a pattern suggestive of UC, 3 of CD and 3 were classified as IBDU. Severity at onset was moderate in 75%. Four patients had concomitant liver disease, one arthritis and one vasculitis. Induction treatment included salicylates (18), steroids (11) and anti-TNF (4). Exclusive enteral nutrition was used in 2 with CD-like pattern, being effective in one. Immunomodulators were initiated at diagnosis in 13 patients. During the evolution, 4 patients needed escalation to anti-TNF. Vedolizumab was used in 2 after anti-TNF primary failure. Colectomy was performed in 5 (20%), in one case more than ten years after diagnosis. Only one of our patients was diagnosed with a specific non-classical-IBD disease (X-linked immunodeficiency), although we have recently included all the other patients in a wide-genetic study to rule out other forms of monogenic diseases, results pending.

Conclusion: VEOIBD present with extensive colonic involvement, moderate to severe activity, and aggressive behavior. Immunological and genetic studies are recommended to exclude specific immunological diseases of similar presentation that can benefit from a different therapeutic approach.

Keywords: Very–Early-Onset Inflammatory Bowel Disease


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Background and Objectives: Atypical phenotypic feature and variable presentation of very early-onset inflammatory bowel disease (VEO-IBD) challenge its diagnosis and management. Useful classification of VEO-IBD would facilitate diagnostic process and eventually improve its management. Our patients with VEO-IBD were evaluated using a phenotypic classification.

Methods: IBD database of a Japanese children’s hospital was retrospectively reviewed. Patients with VEO-IBD were classified into 3 groups by its phenotype; ulcerative colitis type (UCT), non-UC type with perianal disease (NUC-PD), and non-UC type without PD (NUC-NPD). Their disease extent/location, associated condition, diagnostic workup, medical/surgical treatment, and prognosis were reviewed.

Results: There were 38 children with VEO-IBD; 12 UCT, 10 NUC-PD, and 16 NUC-NPD.

All UCT had pancolitis. 2 with primary sclerosing cholangitis were both steroid dependent. 5 children with special health care needs (CSCHN) were all refractory to conventional treatment. 5 required infliximab, and 2 underwent colectomy. One CSCHN died with respiratory failure.

6 NUC-PD were chronic granulomatous disease (CGD) associated colitis, and 5 underwent bone marrow transplantation for its refractoriness. Other 4 NUC-PD underwent next generation sequencing (NGS), which had not revealed monogenic IBD. These 4 required infliximab to control their PD, however; surgical diversion is being considered in 2 for anal dysfunction and recto-vaginal fistula.

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14 NUC-NPD had disease beyond colon. One with lymphocytic intestinal leiomyositis and one with autoimmune enteropathy were diagnosed based on their autoantibodies and histopathology. 4 had strictureing disease, and one of them required ileostomy. 2 with suspected but non-confirmed primary immunodeficiency died of sepsis. NGS tested in 7 had not revealed monogenic IBD.

Conclusions: The phenotypes of VEO-IBD varied, however; our classification was useful to categorise patients with its phenotypic and clinical features. Further utilization of the classification in larger setting would verify its validity in diagnosis and management of VEO-IBD.

Keywords: VEO-IBD, classification, immunodeficiency

EP13. Phenotypic features and long-term outcomes of pediatric inflammatory bowel disease patients with arthritis and arthralgia

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Introduction: The natural history of pediatric inflammatory bowel disease (IBD) patients with joint involvement has not been clearly described.

Aims: To investigate phenotypic features and clinical outcomes of this distinct association.

Materials and Methods: The medical records of pediatric IBD patients diagnosed from 2000 to 2016 were reviewed retrospectively. Main outcome measures included time to first flare, hospitalization, surgery and biologic therapy.

Results: Of 301 Crohn's patients (median age 14.2 years), 37 (12.3%) had arthritis while 44 (14.6%) had arthralgia at diagnosis. Arthritis and arthralgia were more common in females (p=0.028). Patients with arthritis and arthralgia demonstrated lower rates of perianal disease (2.7% and 4.5% vs. 16.9%; p=0.013), whereas patients with arthritis were more likely to be treated with biologic therapy (HR=2.05, 95% CI 1.27-3.33, P=0.009). Of 129 patients with ulcerative colitis (median age 13.7 years) 3 (2.3%) had arthritis and 16 (12.7%) had arthralgia at diagnosis. Patients with arthralgia were treated more often with corticosteroids (p=0.03) or immunomodulators therapies (p=0.003) compared with those without joint involvement. The likelihood to undergo colectomy was significantly higher in patients with arthralgia (HR 2.9, 95% CI 1.1-7.4; p=0.04). During follow-up (median, 9.0 years), 13 patients developed arthritis (3.3%). Arthralgia at diagnosis was a significant predictor for the development of arthritis during follow-up (HR 9.0, 95% CI 2.86-28.5 p<0.001).

Conclusions: Pediatric IBD patients with arthritis have distinct phenotypic features. Arthralgia at diagnosis is a predictor for colectomy in ulcerative colitis and as a risk factor for the development of arthritis during follow-up.


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Background and objectives: Exclusive enteral nutrition (EEN) and partial enteral nutrition paired with the crohn’s disease exclusion diet (PEN+CDED) have been successful first line therapies for pediatric crohn’s disease, inducing early remission. We had previously determined that the microbiome of patients on these two diet therapies were not significantly different from each other at the beginning or the end of treatment. Both diets did however result in significant changes in the microbiome between the start and end of treatment. We were interested in examining how these changes in the microbiome related to changes in functional genes of the microbiome over the course of treatment on these two diets.

Methods: Shotgun metagenome sequences were examined for functional gene assignment (KOs) as well as taxonomic assignment using marker genes from all patients reaching remission on one of the two diet therapies. Statistical tests (Kruskal-Wallis H test with Benjamini Hochberg correction) comparing the start and finish of diet were used.

Results: We determined that ~10% of the KOs identified were significantly different (q<0.05) between the start and end of treatment. The majority of genes (~85%) decreased over the course of treatment. These genes included: two-component system genes used for sensing external signals, butanolate metabolism, genes involved in menaquinone synthesis, and tRNA thiolation, as well as genes involved in sensing and reducing nitrate to nitrite. Genes that increased included: those involved in pyruvate metabolism, heat shock proteins, and amino transferase genes.

Conclusions: Many of the genes identified to have decreased over the course of treatment are found predominantly or exclusively in Proteobacteria. This group of bacteria also significantly decreased over the course of treatment. Additional analyses are being performed to further investigate if specific taxa can be identified that correlate with the changes in functional genes.

EP15. Colonic mucosal cytokine profile (cmcp) after remission treatment with granulocyte/monocyte apheresis (gma) in children with first onset inflammatory bowel colitis

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Backgrounds and Objectives: The inflammatory process in IBD involves the activation of innate immune cells. GMA selectively removes circulating granulocytes and monocytes which are the main producers of pro-inflammatory cytokines. The cytokine profile in the intestinal mucosa in children with IBD is fairly unknown. We have studied the clinical effect and changes in CMCP after GMA treatment together with mesalazine as induction therapy in treatment naïve children with first onset IBD colitis.
Methods: Thirteen children (median age 14.4, range 12.3-15.9 years) with first onset IBD colitis (11 UC and 2 CD) were included in the study. Biopsies for study purpose were harvested from the most and the least inflamed colonic segment. Ten GMA sessions were performed during median 6.25 (range 4.5-8.0) weeks combined with mesalazine (39-65 mg/kg/day). We evaluated disease activity (PUCAI), endoscopic scoring (Mayo), biochemistry tests (blood and feces) and CMCP by real time PCR at diagnosis and at control colonoscopy (CC) 12 weeks after the tenth GMA session.

Results: Twelve patients completed ten GMA sessions and continued mesalazine thereafter. We performed CC in median 93 (range 62-122) days after completion of the GMA treatment. A significant decrease was seen in PUCAI (p=0.004), Mayo endoscopic score (p=0.006), biochemical inflammatory markers, and eight of twelve children reached clinical remission. There was a significant decrease in CSF-2 (p=0.018), TNF-α (p=0.028) IL-23α (p=0.043), IL-1β (p=0.028), IL-36γ (p=0.018), IL-10 (p=0.028), and TGFβ1 (p=0.043) after treatment.

Conclusion: Mucosal pro-inflammatory cytokine levels decreased after GMA together with mesalazine, which may reflect the removal of circulating innate immune cells. We speculate that these findings may explain the observed clinical efficacy observed in a majority of the children.

Keywords: Apheresis, children, IBD, remission, cytokines

EP16. NUDT15 polymorphisms are associated with time-to-leukopenia in korean pediatric inflammatory bowel disease patients under treatment with thiopurines

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Introduction Polymorphisms in the NUDT15 gene are associated with thiopurine-related myelosuppression in patients with inflammatory bowel disease (IBD).

Aims To investigate factors associated with leukopenia and time-to-leukopenia including NUDT15 polymorphisms in Korean pediatric IBD patients during treatment with thiopurines.

Materials and Methods This retrospective study was conducted in 167 pediatric IBD patients who had performed NUDT15 genotyping and had been treated with azathioprine (AZA) from January 2006 to August 2016. Subjects were divided into 3 groups according to NUDT15 activity; normal activity (wild type), intermediate activity (heterozygous at a single variant with one prototype allele) and low activity (with both variant allele). The lowest white blood cell count during AZA treatment, 6-thioguanine nucleotide (6-TGN) levels, AZA dosage, concomitant drug usage, TPMT polymorphism status, and other clinicodemographic factors were investigated.

Results NUDT15 groups of normal, intermediate, and low activity consisted of 71% (119/167), 27% (45/167), and 2% (3/167) of the subjects, respectively. Leukopenia was observed in 16% (19/119), 44% (20/45), and 100% (3/3) of the normal, intermediate, and low activity groups (p<0.001). Among patients with leukopenia, 6-TGN levels were significantly lower in patients with low activity compared to intermediate activity (median 91.8 vs. 365.6, p=0.025) and to normal activity (median 91.8 vs. 308.3 pmol/8×108 RBC, p=0.024). According to multivariate Cox proportional hazard regression analysis, NUDT15 intermediate activity and low activity were each associated with time-to-leukopenia (HR=4.906, 95% CI=2.521-9.548, p<0.001, and HR=102.931, 95% CI=22.353-473.966, p<0.001, respectively).

Conclusions NUDT15 polymorphism is the major factor associated with thiopurine-related leukopenia and time-to-leukopenia in Korean pediatric IBD patients under AZA treatment, which is independent of 6-TGN levels. Genetic evaluation of the NUDT15 gene is required in order to prevent leukopenia during AZA treatment.

EP17. Shifting the Shunters in a Pediatric Inflammatory Bowel Disease Population (pIBD): Thiopurine Dose Splitting versus Allopurinol and Thiopurine co-therapy

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Background and Aim The use of 6-Thioguanine nucleotide (6-TGN) levels has improved safety in PIBD. Our aim was to evaluate the therapeutic outcomes of PIBD patients treated with either Thiopurine dose splitting (Group 1) or Allopurinol and Thiopurine co-therapy (Group 2), for abnormal level outside the therapeutic range of 235 to 450 pmol/8x10E8 RBC and/or abnormal 6-TGN/MeMP ratios (>11). Both are effective treatment options, however there is paucity of data in PIBD. Method 136 patients (Male n=81, age range 4years 10months – 16y 8m, median 13y) were retrospectively identified over a 26 month period.101 (74 %) had normal levels/ratios. The above regimes were implemented on abnormal result, n=35 (26%). Results In Group 1, n=22 patients pre-intervention 6-TGN levels had a median of 199; post-intervention 245. Pre-intervention ratio, median 14.5, post-intervention 5. 18/22 patients had a ratio of >11, in 17/22 (77%) the ratio median drop was 11, the biggest drops were with pre-intervention ratios of >18, with 19/22 (86%) patients returning to ratios <11. Pre-intervention MeMP levels, median of 3179, range 219-5902, post intervention 1496, range 143-3805. In Group 2, n=13 patients pre-intervention 6-TGN levels had a median of 186; post-intervention 309. The pre-intervention ratio had a median of 15; post-intervention 1; 12/13 (92%) patients had a ratio of >11, in those the ratio median drop was 14, with 11/12 having median ratio of 1; Pre-intervention MeMP levels had a median of 2539, post intervention 246. There was a statistically significant difference regarding 6-TGN levels in the split dose versus co-therapy (0.04) and in the drop in ratio (0.013) favoring the co-therapy treatment. Conclusion In our patient cohort both groups lowered abnormal levels/ratios, co-therapy treatment was superior to split dose regimens. Low-dose Thiopurines and Allopurinol co-therapy is safe and effective in PIBD, however needs close monitoring to avoid myelotoxicity.

AzathioprineAllopurinolSplit-dose
EP18. Predicting thiopurine-associated adverse effects in Asian Pediatric inflammatory bowel disease (PIBD) and autoimmune hepatitis patients with NUDT15 mutations

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Background and objectives: Thiopurine-induced leucopenia is one of the known side-effects of azathioprine therapy, and is more common in Asians. Thiopurine methyltransferase (TPMT) genotyping prior to initiation of thiopurine therapy has been advocated. Although TPMT mutants are rare amongst Asians, Nudix Hydrolase(NUDT)15 mutants are relatively more common. We aim to describe the influence of NUDT15 mutations on adverse effects to azathioprine therapy.

Methods: We performed pilot NUDT15 mutation testing in 19 patients with PIBD and/or autoimmune hepatitis requiring azathioprine. Three main genetic variants of NUDT15 were tested: c.415C>T, c.52G>A and c.36-37insGGAGTC. We analysed the maximum dose of azathioprine tolerated, the lowest white cell count(WBC), absolute neutrophil count(ANC) and absolute lymphocyte count(ALC), as well as other side-effects experienced.

Results: 6 patients carried NUDT15 mutations and were all TPMT non-mutants: 1 patient is a homozygote for c.415C>T variant [*3/*3], and experienced (i)severe neutropenic sepsis (lowest absolute neutrophil count 0.06; total white count 2.22) requiring G-CSF support within 2 weeks of azathioprine initiation of 2mg/kg/day, and (ii) severe alopecia areata. 2 patients were heterozygotes for c.415C>T [*1/*3] and tolerated azathioprine dose escalation to 2.5-3mg/kg/day; only transient lymphopenia (lowest absolute lymphocyte count < 1.0) without leucopenia was reported with 1 c.415C>T heterozygote.

3 patients were heterozygotes for the following variants: G52A variant[*1/*5], c.36-37insGGAGTC[*1/*6], and both c.36_37insGGAGTC and C415C>T(double heterozygote)[*1/*2]. These heterozygotes tolerated dose increment to 2.3-2.8mg/kg/day without onset of leucopenia. The patient with both c.36_37insGGAGTC and C415C>T mutations[*1/*2] experienced telogen effluvium (alopecia).

Conclusions: Homozygotes for c.415C>T variant[*3/*3] may experience severe neutropenia and alopecia, while heterozygotes in our pilot sample appear to tolerate azathioprine escalation to therapeutic dose ranges with minimal side-effects except for 1 double heterozygote experiencing alopecia. NUDT15 testing is more predictive of thiopurine-induced leucopenia and alopecia than TPMT genotyping.

EP19. Myelotoxicity after primate infection with epstein-barr virus in pediatric inflammatory bowel disease patients treated with thiopurines

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Background and objectives: Thiopurines are frequently used to maintain remission in Pediatric IBD. Primary Epstein-Barr virus (EBV) infection on this treatment has been associated with severe hematological complications. Methods: Retrospective study of hematological complications occurring in our IBD patients treated with azathioprine (AZA) secondary to primary infection by EBV (diagnosed by serology and viral load). Clinical and analytical parameters, treatment strategy and outcomes were collected.

Results: 6 patients (4 Ulcerative Colitis, 2 Crohn’s Disease) were included. Mean age at EBV infection 15.5 years (Range 13-18). Acute symptoms at presentation: fever (100%), adenopathies (100%) and sore throat (65%). Mean duration of fever before being investigated 8.16 days (range 3-10 days). Mean baseline EBV load: 7,628 copies/ml (range 265-16,954 copies/ml). Leukopenia was present in all the patients (range 1,300-2,600/mm3); mean absolute neutrophil count 134/mm3 (Range: 500-1,700/mm3). Other findings: high ferritin levels (>150 ng/ml) in 83.3%, high lactate dehydrogenase (>70 IU/L) in 100%, 5/6 patients required hospital admission. 1/6 was performed a bone marrow biopsy that excluded hemophagocytic lymphohistiocytosis. Intravenous Ganciclovir was initiated in all patients (mean duration: 17 days; range 7-21 days). None of the patients developed hemophagocytic syndrome or lymphoma. AZA was discontinued in 5/6. One patient received intravenous gammaglobulins due to slow improvement of the symptoms, being maintained after with 5-ASA (rejection to start anti-TNF). Other CD patient started anti-TNF on monotherapy with good response. AZA was re-started in the other 3 patients after viral negativization, without complications. In one patient AZA dose was decreased without complete withdrawal, with improvement and subsequent dose increase.

Conclusions: Pediatric patients on thiopurines and primary infection by EBV are at increased risk for developing myelotoxicity that can be severe even fatal. In our patients, antiviral treatment and suppression or decrease of AZA doses seems to be an adequate strategy to avoid major complications.
EP20. Are disease activity, illness perceptions, coping, anxiety, and depression related to quality of life in youth with inflammatory bowel disease?

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Background and objectives In adolescence and early adulthood, clinical symptoms of inflammatory bowel disease (IBD) are related to inflammation but also to illness perceptions, coping, anxiety, and depression, and health-related quality of life (HRQOL). This complex interplay makes medical as well as psychological treatment of these patients necessary but challenging. We aim to investigate these relationships based on the Common Sense Model (CSM) of illness.  

Methods Data on clinical disease activity, illness perceptions, coping, anxiety, depression, and HRQOL were collected in 374 adolescents and young adults (age 10-25, 44.1% male) with confirmed IBD. We tested the interrelationships between all variables in three age groups (10-17, 18-20, 21-25 years) using path analyses. We pooled the results of the three groups to establish a final overall model.  

Results Elevated symptoms of anxiety and depression were found in 44.5% and 18.8% of the patients, respectively. Only in the 10-17 year and 18-20 year age groups, path analyses showed that our data fitted excellent to the CSM. Overall, higher clinical disease activity was significantly associated with more negative illness perceptions. More negative illness perceptions were significantly associated with less favorable coping, anxiety, depression, and lower HRQOL. More depression was significantly associated with lower HRQOL.  

Conclusions Consistent with the CSM, clinical disease activity, negative illness perceptions, maladaptive coping and depression are interrelated and negatively associated with HRQOL in 10-25-year old IBD patients. Remarkably, anxiety and adaptive coping did not influence HRQOL. Psychological interventions for IBD youth should therefore be targeted at negative illness perceptions, maladaptive coping, and depression to improve HRQOL.  

Keywords: inflammatory bowel disease, adolescents, young adults, health-related quality of life, common sense model


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Introduction: Treatment choice should be informed by the patient’s risk for adverse outcomes, such as their risk for relapse, surgery, recurrence after surgery, hospitalization, and poor height. Many studies have reported predictors for these outcomes in children, but a need exists for a summary of these predictors. To address the need for knowledge consolidation in this subject area, we conducted a rapid review with the objective of summarizing the current evidence on the predictors for relapse, surgery, recurrence after surgery, hospitalization, and poor height in the pediatric Crohn’s disease population  

Material and methods: A rapid review based on Cochrane methodology of the literature was performed. This rapid review followed the same protocol as a systematic review, but limited the search strategy to include only one database and no grey literature. The Ovid MEDLINE database was searched. The search was limited to studies published in English from the year 2006 to June 2016. Key search terms included were “Crohn Disease”, “pediatric”, “predict”, “growth”, “recurrence”, “hospitalization”, and “surg”. The quality of studies was assessed with the Newcastle-Ottawa Scale. 

Results: Out of a 1497 records identified through the initial search, 101 met the inclusion criteria and were included in this analysis. The majority of studies commented on predictors of surgery (Fig. 1). Relapse risk was outlined in Fig. 2. Surgical risk was outlined in Fig. 3. No obvious risk predictors for hospitalization, disease recurrence after surgery and poor height were found.  

Conclusion: Strong support exists for using the presence of stricturing or penetrating disease behaviour in patient risk stratification for surgery, while some support exists for the use of bowel disease location in risk stratification. There was no support for the use of the patient's PCDAI score in risk stratification, and limited literature existed on pediatric perianal disease and its outcomes.

EP22. Perinatal factors and risk of inflammatory bowel disease in the offspring: a systematic review and meta-analysis

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Background: It has been hypothesized that exposure to environmental factors during critical windows of immune maturation may interfere with the immune system’s development and influence the subsequent risk for inflammatory bowel disease (IBD).  

Objectives: To summarize the available data of the literature and perform a meta-analysis regarding the association between perinatal factors and the subsequent risk for Crohn’s disease (CD) or ulcerative colitis (UC) in the offspring.  

Methods: We systematically searched the following electronic databases: Embase, PubMed, Medline and EBM Reviews to identify observational studies on the association between perinatal factors and IBD in the offspring up to April 2017. A meta-analysis was performed using RevMan 5 to obtain a combined effect measure and the 95% CI with random effects models. Pooled adjusted odds ratios (OR) with 95% confidence intervals were calculated by combining the inverse of their variance for each factor.
Results: Twelve studies (5 cohort studies and 7 case-control studies) were identified out of 1852 studies reviewed. Maternal diabetes during pregnancy was associated with an increased risk for CD [OR(95% CI): 1.67 (1.18-2.36)] but not UC. Maternal age >35 years was associated with an increased risk for CD [1.65 (1.02-2.66)] but a decreased risk for UC [0.92 (0.86-0.98)]. The following perinatal factors were not associated with the risk for IBD: maternal infection, pre-eclampsia, birth weight, preterm, and low APGAR score. (See Table 1.)
Conclusion: This meta-analysis suggests opposite associations between advanced maternal age and risk for CD or UC. In addition, diabetes during pregnancy appears to be associated with an increased risk for CD in the offspring.


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Background and objectives: Calgranulin C (S100A12) is a relatively unknown fecal marker of inflammation that is potentially more specific for IBD than calprotectin, since it is only released by activated granulocytes. We compared calprotectin and S100A12 to see which of the two markers best predicted IBD in children and teenagers with chronic abdominal complaints.

Methods: We performed a multicenter prospective study in 19 paediatric clinics in the Netherlands and Belgium. Eligible patients aged between 6 and 18 years sent a stool sample to the coordinating laboratory for immediate calprotectin measurement (ELISA, BÜHLMANN Laboratories). Calgranulin C was measured at a later stage (INFLAMARK ELISA, CisBio Bioassays). Patients with a high likelihood of IBD underwent upper and lower endoscopy (i.e. reference test), while those with a low likelihood were followed for 6 months for appearance of additional symptoms suggestive for IBD (i.e. alternative reference test). We used Bayesian statistics to correct for verification bias. We evaluated test characteristics for commonly used and best cut-off points.

Results: We included 337 patients of which 142 underwent endoscopy and 195 clinical follow up. Eventually a total number of 9 patients were diagnosed with IBD. When common cut-off points (Calprotectin 50 µg/g and S100A12 0.75 µg/g) were used, S100A12 had better specificity (i.e. less false positives) than calprotectin. When different cut-off points (resp. 400 µg/g and 0.75 µg/g) were used, S100A12 had better sensitivity (i.e. less false negatives). The ROC-curve based cut-off points were used (Calprotectin 400 µg/g and S100A12 0.75 µg/g), both tests performed equally well (figure 1).

Conclusions: Both calprotectin and calgranulin C have excellent test characteristics to select children and teenagers with high likelihood for IBD for endoscopy.

Keywords: screening, S100A12, calprotectin

Figure 1: Test accuracy of (A) commonly used cut-offs (Calprotectin 50 µg/g; S100A12 0.75 µg/g); and (B) ROC-curve best cut-offs (resp. 400 µg/g and 0.75 µg/g).

EP24. Fecal Calprotectin Test Performed at Home – a Prospective Clinical Study in PIBD

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Introduction: To take a fecal sample to laboratory for measurement of fecal calprotectin (FC) is time-consuming. Thus, development of home tests has emerged.

Aims: We aimed to study the use of a FC home test in pediatric patients with inflammatory bowel disease (PIBD) in real life.

Methods: PIBD patients were invited to perform a FC home test IBDoc® once a month for six months and to report their clinical disease activity at testing using a validated symptom questionnaire. At the end, spared fecal samples were analyzed using both ELISA and IBDoc® in the laboratory. The participants filled in a questionnaire concerning their views on FC testing at the start and at the end of the study.
Results: Thirty-five out of 52 (67%); aged 5 to 18 years) completed the 6 months study and altogether 197 home tests were performed. Of these, 15% failed mainly because of technical reasons. Every other patient (47%) considered home-testing comparable or superior to routine testing. On contrary, parents were unsatisfied, mostly because IBDoc® results were significantly different from ELISA and considered the application difficult to handle. However, over 80% of the parents considered that home-testing would improve the management of their child. Conversely, IBDoc® performed by a laboratory professional was comparable with ELISA suggesting that practical issues hampered home-testing. Figure 1 shows the correlation between IBDoc® and ELISA when performed in a laboratory and Figure 2 when IBDoc® was performed at home. In most patients, the clinical disease activity was mild through the study period. In general, the participants were interested in their FC values as shown in Figure 3.

Conclusions: PIIBD patients and their families were interested in FC home-monitoring and willing to take testing as a part of the management but such an approach needs guidance more than anticipated.

EP25. Height-z-score deficit as a measure of linear growth impairment in children presenting with IBD: a canadian multi-centre inception cohort study

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Introduction: An important target in the management of pediatric inflammatory bowel disease (IBD) is normal linear growth. Greater awareness of IBD and more effective therapies are anticipated to reduce the prevalence of linear-growth impairment.

Aim: To evaluate the current magnitude of linear-growth impairment at diagnosis in pediatric Crohn’s disease (CD) and ulcerative colitis (UC).

Methods: Since April 2014, the Canadian Children IBD Network (CIDsCaNN) inception cohort study prospectively enrolled patients aged ≤17 years presenting to 12 centres across Canada. Assessment of linear growth at presentation included height measurement and mid-parental height (MPH) calculation. All growth parameters were standardized utilizing the Centers for Disease Control (CDC) 2000 reference tables. ‘Deficit Height-z-score’ was calculated using the formula: ‘Actual Height-z-score’ minus ‘Predicted Height-z-score’.

Results: Among participants (n=1003, 57% male; CD: 61%, UC: 29%, IBD-U: 10%), median age at presentation was similar for the three disease sub-categories (13.2yrs: IQR 10.8-15.1), but duration of symptoms prior to diagnosis was longer in CD (5 months, IQR 3-112months) vs UC (3 months, IQR 1-6 months) (p<0.001). Disease extent for UC was 76% E4; 10% E3; 14% E1/2 and for CD was: 51% L3; 25% L2; 20% L1. Linear growth impairment, based on historical growth parameters, occurred in 19% of CD patients, and 2% of UC patients. Predicted height-z-scores (based on MPH) were normally distributed (mean 0.08, SD 0.8) with no difference noted between CD and UC patients. The UC cohort had normal height at diagnosis; in the CD cohort height was significantly reduced, consistent with the calculated deficit. Males demonstrated a greater deficit than females (p=0.05) (Table).

Conclusions: Linear growth impairment still occurs prior to the recognition of Crohn’s disease, however its magnitude is less than in previous eras. Deficit in Height-z-score based on MPH appears a useful metric for the contemporaneous quantification of linear growth impairment.

EP26. Body Mass Index in the Lower or Upper Quartile is a Marker of Severe Disease Course in Pediatric IBD Patients.

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Background and objectives: IBD has been historically associated with underweight and malnutrition. Similarly to the general population, obesity is emerging as a significant problem in IBD. It is uncertain how underweight and obesity impact the clinical course of the disease. The aim of our study was to describe the association between body mass index (BMI) at diagnosis to disease course.

Methods: We reviewed the medical records of children with IBD from the pediatric gastroenterology unit, "Dana-Dwek" children’s hospital, in the years 2008-2016. Demographic and anthropometric data was collected as well as disease characteristics, course and treatment. Patients were categorized in quartiles according to BMI percentiles at diagnosis (Q1-Q4). Disease activity at diagnosis was evaluated by PCDAI or PUCAI.

Results: One hundred patients were evaluated: 62 with Crohn's disease and 38 with Ulcerative Colitis (UC). The median age (IQR) at diagnosis was 13.9 (11.9-15.2) years. The median follow up time (IQR) was 7.2 (6.1-8.8) years. The median time before diagnosis was associated with BMI in Q1 and Q4, as well as high disease activity at diagnosis (p<0.001 for both). In a multivariate analysis, BMI in the lower and upper quartiles was associated with shorter time to exacerbation (HR 3.2 and 4.7, respectively, p=0.016) and use of biologic drugs (HR 4.5 and 4, respectively, p=0.021). There was no association between BMI and need to use steroids, immunomodulators and hospitalization.

Conclusions: BMI in the lower and upper quartiles was associated with more severe disease course in children with IBD. BMI may serve as an easy and available predictor of IBD prognosis.
EP27. Successful use of the ImproveCareNow (ICN) Quality Improvement Tool: Our 7 year outcomes and achievements

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ImproveCareNow (ICN) is a Quality Improvement (QI) Program. ICN uses patient data to drive improvements in the care and health of PIBD patients. It’s a network of 96 international centers with over 27,000 PIBD patients, that benchmarks care against agreed targets. We share our 7 year experience in using this QI tool.

All eligible IBD patient enrolled in the program had their data collected at clinic visit and ambulatory review. Pre-visit planning meetings were held to discuss all patients prior to the visit. The data that is entered consists of diagnosis, using the Paris classification, growth and nutrition, lab results, medications, physical assessments, disease activity and extra intestinal manifestations. Data from each visit was analyzed and reports were generated within 24 hours. Each patient’s results were stratified and scored weekly, so that individual treatment plans could be instigated. Reports were reviewed on a monthly basis and changes to clinical management were implemented on an individualized basis, adhering to local treatment policy. Monthly QI meetings set and reviewed 90 day goals, enabling the team to strive for better results.

At present 138 (61 female, mean 12.6 y) patients are registered in the database. Patient who have been transitioned are excluded. Overall remission rate increased from 60% in to 72% in, Steroid free remission rates from 50 to 71%, patients off steroids from 60 to 98%, satisfactory growth status from 92 to 93%. Patients in nutritional failure from 9 to 0%. Before joining ICN we did not know patient numbers and did not do any pre-visit planning (PVP), now we have all our IBD patients registered and we do PVPs on each patient before their clinic review, please see Table attached.

ICN has shown to be an excellent tool of improving quality of care in PIBD, managing treatments and improving outcomes.

EP28. Cognitive debriefing interviews towards developing a patient reported outcome (pro) for pediatric ulcerative colitis (tummy-uc) in a phase 2B study

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Background and aim: Under the qualification program of the FDA and EMA, we aimed to develop a Patient Reported Outcome (PRO) measure of signs and symptoms for pediatric ulcerative colitis (UC) (i.e. the TUMMY-UC index) for use in trials and clinical practice. We previously developed a draft TUMMY-UC via concept elicitation qualitative interviews. Here we report the results of the cognitive evaluation for formatting and weighting of the index.

Methods: We performed cognitive debriefing interviews with 30 children with UC and caregivers (for those ≤5 years old); age 11.5±4, range 2-17 years; 33% males; 27% with moderate-severe disease and 53% in remission; 78% with extensive or pan-colitis), in Israel, England, Ireland, Canada and the USA, thus ensuring cultural diversity. We compiled contending scales for each item and explored the vocabulary children prefer.

Results: In 98% of cases children had full understanding of the questions and responses. 88% understood the meaning of “last 24 hours since this time” as a recall period. The exact response options were amended based on the obtained feedback. All children younger than 11 years preferred the FACES pain scale and most adolescents preferred the 100mm VAS version, thus both were retained. Items were ranked in the following order of importance by the children on a ‘1’ (least important) to ‘5’ scale: amount of rectal bleeding (4.5), rectal bleeding frequency (4.2), stool frequency (4.1), abdominal pain (3.9), stool consistency (3.6), urgency (3.6), nocturnal stools (3.5) and fatigue (3). Reassuringly, the same rank-order was recorded for children younger than 11 years.

Conclusions: In this phase 2B, the exact wordings of the 8 TUMMY-UC items were revisited for optimal vocabulary. The importance grading has assigned the weighting of the items. The TUMMY-UC will now be validated and evaluated for cutoff scores in a phase 3 study.

EP29. Planned transition of adolescent IBD patients from pediatric to adult care results in higher remission rates

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Introduction: Increasing number of adolescents need handover to adult care due to increasing incidence of pediatric-onset inflammatory bowel disease (IBD). Whereas transfer is essentially only an event, transition is a well-planned, coordinated process. Recent data support that structured transition programs in IBD may improve patient compliance and disease control.

Aims: To evaluate the impact of our transition program introduced 3 years ago on clinical outcomes in adolescent IBD patients diagnosed in pediatric care.

Methods: In this retrospective study patients within the last 2 years before our transition program introduced (Group A) were compared to those who entered the planned transition service (Group B). Outcomes at 1 year after handing over to adult care were evaluated.

Results: 39 IBD patients diagnosed before the age of 18 were identified (16 male, 23 female; 33 Crohn’s disease, 6 ulcerative colitis). 23 patients (Group A) were transferred to adult care without transition, whereas 16 patients attended transition clinics before transfer (Group B). When comparing Group A patients to Group B mean age at diagnosis (15.08 vs. 13.38 years, p=0.037), disease duration before transfer (40.57 vs. 54.81 months, p=0.16), disease phenotype at diagnosis, BMI at transfer (20.13 vs. 21.2, p=0.463), disease status at transfer (19 vs. 14 patients were in remission, p=0.681), anti-TNF therapy usage at transfer (9 vs. 7 patients, p=0.773) and at 12 months after transfer (3 vs. 6, p=0.259) did not differ significantly in the two groups. Significantly higher number of Group B patients were in remission at 12 months follow up after transfer when compared to patients in Group A (15 vs. 11, p=0.011).

Conclusions: Our transition program resulted in higher disease remission rate at 1 year follow-up after transfer to adult care highlighting the need for well-established transition programs in IBD care. Keywords: transition program, remission, adult care
Background and objectives: The incidence of childhood-onset (<18 years) inflammatory bowel disease (IBD) is increasing. At the same time, the medical treatment of these patients has improved, but the effect on the need of surgical treatment during childhood as well as later in life needs further investigation. We aimed to examine the surgical treatment of childhood-onset IBD during years before and after the introduction of biologics.

Methods: In a cohort study based on nation-wide registers with prospectively recorded information we identified 6377 children (<18 years) diagnosed with incident IBD in 1990-2014 through the Swedish Patient Register. IBD in 1990-2014 respectively. Abdominal surgeries (intestinal resections and colectomies) and perianal surgeries were identified through the Swedish Patient Register. The cumulative incidences of surgeries were calculated using the Kaplan Meier method. Multivariable Cox regression models were used to calculate the risk of surgery.

Results: In the cohort, 43% were girls and 57% boys. The cumulative incidence of intestinal surgery is summarized in figure 1. Cumulative incidence after three calendar years (17% and 5% in patients diagnosed in 1990–1996 and 2010–2014, respectively).

Conclusion: Over the last 25 years, the cumulative incidence of abdominal surgery in childhood-onset IBD has decreased by almost 50%. Over all calendar periods, patients with the earliest IBD-onset had the lowest cumulative incidence of surgery.

Key words: Inflammatory bowel disease, Crohn’s disease, ulcerative colitis, children, surgery

Figure 1: Cumulative incidence of intestinal surgery in childhood-onset inflammatory bowel disease by phenotype, age at first IBD-diagnosis, year of first IBD-diagnosis, and sex. Counts represent number of patients at risk at a certain time-point.
Background: Exclusive enteral nutrition (EEN) has been shown to be more effective than corticosteroids in achieving mucosal healing in children with Crohn’s disease (CD) without having their side effects. Objectives: The aims of this study were to determine the efficacy of EEN in terms of inducing clinical remission in newly diagnosed CD children and to describe the predictive factors of response to EEN. Materials and methods: An observational retrospective multicenter study including newly diagnosed CD pediatric patients who received EEN. Results: Two hundred and eleven patients (130 males) from 35 pediatric centres were included; the mean age at diagnosis was 11.6 ± 2.48 years. The median duration of EEN was 8 weeks (IQR 6–8), after that 172/211 (81.5%) achieved clinical remission (wPCDAI < 12.5). The FC levels (mg/g) decreased significantly at the end of EEN period in both groups (responders: 764 IQR (281-1364) vs 588 IQR (281-1364) p=0.01; non-responders: 1108 IQR (660-2574) vs 588 IQR (281-1364) p=0.013. As is shown in table 1, patients with wPCDAI ≤ 57.5, FC < 500 mcg/g, CRP > 10 mg/L and ileal involvement tended to response better to EEN. Conclusions: EEN administered for 6-8 weeks is effective for inducing clinical remission. Although some patients will respond better, EEN should be used as the first line therapy in luminal pediatric Crohn’s disease independently of the age at diagnosis, the location of the disease and the value of wPCDAI.

Table 1. Predictive variables of response to EEN. Multivariate analysis. Dependent variable: wPCDAI < 12.5. n=211 patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (CI 95%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>wPCDAI ≤ 57.5 (not severe)</td>
<td>3.727</td>
<td>0.01</td>
</tr>
<tr>
<td>Fecal calprotectin &lt; 500 mcg/g</td>
<td>4.440</td>
<td>0.030</td>
</tr>
<tr>
<td>CRP &gt; 10 mg/L</td>
<td>2.925</td>
<td>0.019</td>
</tr>
<tr>
<td>Ileal involvement</td>
<td>2.641</td>
<td>0.063</td>
</tr>
</tbody>
</table>

* Hosmer and Lemeshow test: p=0.865; R² Nagelkerkes: 0.171; Sensitivity: 96.52 (91.6–98.7); Specificity 21.62 (10.42–38.6); PPV: 82.73 (75.98-87.95); NPV: 38.46 (15.13-67.7).

EP32. Trough levels to Infliximab at W6 are predictive of remission at W14, in pediatric Crohn’s disease.

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Aims: This retrospective study aimed to analyse factors associated with remission after 14 weeks of induction treatment by IFX in children with CD. Methods: All patients aged from 2 to 18 years old with CD meeting European Crohn’s and Colitis Organisation criteria and treated for the first time by IFX between January 2002 and March 2014 at a single tertiary pediatric center were considered for inclusion in this retrospective study. Results: We analyzed 107 patients with CD, with a total of 428 visits until W14. The principal reason to start infliximab was failure of immunosuppressive therapy (60%). Infliximab proved to be an effective treatment in our cohort since 75.7% (n=81) patients were responders to infliximab and 40% (n=42) were in clinical remission whereas 24.3% (n=26) were non respondents at W14. At week 14, 107 patients were divided in three groups related to the clinical activity of their disease: lack of clinical response, partial clinical response, clinical remission. Major baseline characteristics were not associated with clinical remission: sex, age at diagnosis, disease location, time between diagnosis and induction, age at induction. Drugs associated with infliximab at W0, W2, W6 or W14, whether it was immunosuppressive agents or corticoids were not associated with remission. Patients with low albumin levels had a worse response at induction. Trough residual of infliximab > 8.5 µg/ml at w6 increase of 11.3 times the risk to obtain clinical remission at w14. Lack of growth retardation at induction increased of 3.98 times the risk to obtain clinical remission at w14. Conclusion: Infliximab measurement in combination with evaluation of clinical severity (low body weight, growth retardation, hypoalbuminemia, severe disease) appears to be a reasonable strategy for predicting both short- and long-term treatment outcomes with IFX in the initial stage of treatment.

Vol. 65, Supplement 1, October 2017
EP33. Infliximab trough levels and mucosal healing are associated with sustained clinical remission after infliximab cessation in pediatric Crohn’s disease patients

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Introduction: There is limited data regarding the clinical course of Crohn’s disease (CD) after discontinuing infliximab (IFX) treatment in the pediatric population.

Aims: To investigate the outcome of pediatric CD patients who had discontinued IFX under clinical remission by combined immunosuppression with IFX, and to reveal risk factors associated with clinical relapse in these patients.

Material and Methods: We conducted a retrospective observational study from January 2009 to June 2016 at the Department of Pediatrics, Samsung Medical Center. The subjects were 63 patients who had discontinued scheduled IFX under sustained corticosteroid-free clinical remission for at least 1 year by combined immunosuppression with IFX and azathioprine, and had been followed for at least 1 year after IFX cessation. Relapse free survival rate and the median time to relapse was estimated by Kaplan-Meier survival analysis. Demographic, clinical, biochemical, and endoscopic factors at IFX cessation were evaluated for their association with clinical relapse using Cox proportional hazard regression analysis.

Results: After a median follow-up period of 4.3 years (range: 1-7.5 years), 60% (38/63) patients had experienced a clinical relapse. The estimated cumulative relapse rate for 1-, 2-, 4-years were 19%, 36%, and 62%, and the median relapse time was 3.3 years from IFX cessation. According to multivariable Cox proportional hazard regression analysis, IFX trough levels of ≥2.5 μg/mL and incomplete mucosal healing were associated with clinical relapse (HR=7.199, 95% CI=1.641-31.571, p=0.009, and HR=3.628, 95% CI=1.608-8.185, p=0.002, respectively). Retreatment with IFX was effective in 33 patients (92%).

Conclusions: Approximately 50% of patients with pediatric CD under sustained clinical remission for at least 1 year by combined immunosuppression will experience a relapse within 3.3 years after IFX cessation. A subgroup of patients with subtherapeutic IFX trough levels and a complete mucosal healing at IFX cessation may better sustain clinical remission under thiopurines after IFX discontinuation.

EP34. Biological therapy in inflammatory bowel disease evaluation of the “quick step-up” protocol

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Introduction Biological therapy is an important option in the treatment of inflammatory bowel disease (IBD). The option for top-down is not yet validated in pediatric population, on the other hand, step-up protocol can compromise the early control of the disease. Some studies suggest that evolution may be more favorable when biologicals are used early. This study aims to validate the quick step-up protocol.

Methods Retrospective analysis of the clinical processes of patients with IBD undergoing pediatric consultation at Centro Hospitalar de São João( January 1999 - October 2016).

Results 280 cases of inflammatory bowel disease: 68% Crohn’s disease (DC), 28% Ulcerative Colitis (UC) , 4% Indeterminate Colitis. Biological drug therapy was prescribed in 36% of patients. The median age at diagnosis of these patients was 13 years (M: 66%, F: 33%). The time from diagnosis to the start of biological therapy was less than 2 years in 78% of the cases, and of these 72% started during the first year. In 83 patients with CD, the main indication for biological treatment was to meet criteria for quick step-up (55%), to maintain active disease despite optimized immunomodulatory therapy (15%) and to have severe perianal disease (10%). In the 18 patients with UC, the main indication for biological treatment was to meet criteria for quick step-up (55%). In 101 patients on biological therapy, one had primary failure on infliximab and 5 lost it’s therapeutic response.

Conclusions The current “quick step-up” protocol allows the identification of cases that do not respond to conventional treatment and promote disease control in the window of opportunity that may prevent excessive degradation or progression of the disease. About 2/3 of patients are thus spared from early exposure to biological drugs, maintaining adequate disease control with other drugs. Keywords: Inflammatory Bowel Disease; Biologicals; Quick step-up


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Introduction The relatively high cost and patent expiry of infliximab, an anti-tumor necrosis factor monoclonal antibody used in inflammatory bowel disease (IBD), has led to the development of biosimilar versions of the reference product (RP). The biosimilar CT-P13 has been approved worldwide for all indications held by the infliximab RP.

Aim To investigate the long-term efficacy, safety, pharmacokinetics, and immunogenicity of CT-P13 after switching from infliximab RP in patients with pediatric-onset IBD.

Materials and Methods In this prospective, observational study, patients with pediatric-onset IBD aged <18 years at diagnosis were followed for 1 year after switching from infliximab RP to CT-P13. Primary endpoints were the proportion of patients continuously receiving CT-P13 for 1 year post-switch, and the proportion of patients achieving a corticosteroid-free sustained clinical remission without further dose intensification at 1-year post-switch.

Results Thirty-eight patients were recruited, with a median age of 15.1 years (range: 7.6–20.5 years) at infliximab RP initiation. CT-P13 had been continuously received by 35/38 (92.1%) patients at 1-year follow-up, and 29/35 (82.9%) patients experienced a corticosteroid-free sustained clinical remission at 1 year. There were no statistically significant differences between any measures of disease activity, pharmacokinetics, or immunogenicity at the time of switch and at 1-year post-switch. A total of 30 adverse events occurred during the 1 year follow-up. However, no serious adverse events or infusion related adverse events occurred.

Conclusions In real-life practice, switching from maintenance infliximab RP to CT-P13 did not result in any significant differences in efficacy, pharmacokinetics, or immunogenicity in patients with pediatric-onset IBD and no unexpected safety issues, supporting findings from randomized controlled trials.
EP36. Maintenance biosimilar Infliximab therapy in Crohn’s Disease Pediatric patients after switching from original molecule.

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Background: Biosimilar infliximab was authorized in European Union in 2014. More often, biosimilars are only infliximab molecules available in hospitals. Because of this, switching between originator and biosimilar is only possible option for continuing biological therapy.

Aim: The aim of the study was assessment of efficacy maintenance therapy among patients switched to biosimilar during one course of therapy.

Methods: Sixteen Crohn’s disease paediatric patients who were switched from originator to biosimilar infliximab (CT-P13) were included in the study. The patients were assessed before switching, after one and/or second year of therapy. Disease severity assessed by PCDAI scale, laboratory values (CRP, ESR, platelet count, haemoglobin level) were recorded. AE were recorded.

Results: At the time of switching mean PCDAI was 9.2 (median 7.5; 0-35). Assessment after one year therapy was performed in 12/16 (75%) patients. All patients were in clinical remission. Mean PCDAI score after one year therapy was 2.29 (1.25; 0-7.5). Four patients were discontinued from therapy in different period of time after switching. Three of them achieve 18 years of age and were transferred o the adults medical centers. One patient have been changed to adalimumab because of psoriasis suspicion. Eight patients were also assessed after 2 years from switching. Mean PCDAI score was 2.8 (0; 0-10). Rest of the patients – 4, finished the therapy between first and second year after switching. Two were transferred to the adults medical centers, one 1 patient had SAE (pneumonia which resulted in Crohn disease exacerbation), 1 patient lost response to Infliximab and was qualified to surgical treatment. The occurrence of sporadic mild adverse events did not differ before or after switching and was consistent with INF molecule safety profile.

Conclusion: Switching form originator to biosimilar infliximab in children with CD seems to be safe.

EP37. Efficacy and safety of adalimumab after infliximab failure in pediatric ulcerative colitis: a real-life experience from the sigepn-IBD registry

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Introduction: No pediatric data on the efficacy and safety of adalimumab (ADA) in pediatric ulcerative colitis (UC) are available.

Aims: The objective of the present study was to evaluate the effectiveness and safety of ADA in children with UC who experienced previous infliximab (IFX) failure or intolerance.

Materials and methods: This retrospective study included all children with UC from a national pediatric registry who received ADA therapy. The primary endpoint was the rate of corticosteroid (CS) free remission (PUCAI<10) at week 52. Secondary outcomes were: the rate of continuous clinical response and remission, primary non-response and loss of response at Weeks 12, 30, and 52 and rate of mucosal healing at week 52.

Results: Of 514 patients with UC included in the registry, a total of 32 children (6%) with UC received ADA (median age 10±4years). Median disease duration before ADA therapy was 27 months. All patients received previous IFX therapy (43% intolerant, 50% non-responders, 7% positive anti-IFX antibodies). Fifty-two weeks after ADA initiation 13 patients (41%) were in CS-free remission. MH occurred in 9 patients (28%) at 52 week. The cumulative probability of clinical relapse-free course was 69%, 59% and 53% at 12, 30 and 52 weeks, respectively. Ten patients (31%) had a primary failure and 5 (15%) loss of response to ADA. No significant differences in terms of efficacy were reported between not responders and intolerant to IFX to (p=1.0). Overall, nineteen patient (59%) maintained ADA therapy during 52-week follow-up. Seven patients (22%) experienced an adverse event. No serious side effects were observed and none resulted in ADA discontinuation.

Conclusions: In this cohort of children with UC ADA had a favorable short- and long-term efficacy, allowing to recover a significant percentage of patients intolerant or not-responding to IFX. The safety profile was good.

EP38. Efficacy and safety of vedolizumab treatment in Pediatric patients with inflammatory bowel disease

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Introduction
Efficacy and safety of vedolizumab, has been demonstrated in trials involving adults diagnosed with Crohn's Diseases (CD) and Ulcerative Colitis (UC). In children, it is being used in some selected cases in whom conventional therapy failed, as off-label use. The aim of this study is to investigate the efficacy and safety profile of vedolizumab treatment in paediatric patients.

Methods
Spanish paediatric multicenter observational trial, involving patients that have received treatment with vedolizumab. The percentage of remission and information about clinical and analytical activity at week 6, 14, 30 and 52 were analyzed. Every adverse effect during treatment was recorded.

Results
14 patients were included (9 male, 7 CD). In CD patients, 57% showed growth delay and 14% had penetrating phenotype. In UC patients, 100% had pancolitis, and 87.5% showed severe activity. Considering analytical parameters, CRP values decreased from 4.3 (+/- 1.2) at the beginning to 2.2 (+/- 0.8) at week 14 and 0.13 at week 30. VSG, albumin, haemoglobin, iron and calprotectin also improved. There was initial response at week 6 in 71.4% of UC, whereas in CD this was 28.6%. At week 14, in CD patients this increased to 57%, and in UC it remained in 71.4%. At week 30, 6 patients were still on treatment (3 CD), maintaining response 2 of the CD patients (1 remission), and 3 of the patients with UC. 50% of patients experienced side effects, being more serious in CD.

CONCLUSIONS
Vedolizumab was effective in a high percentage of patients refractory to anti-TNF, and it seems to be more effective as induction therapy in UC than in CD patients. Some adverse reactions were observed in CD patients. More prospective trials are needed to determine efficacy and security of this drug in paediatric population.

EP39. Vedolizumab therapeutic drug monitoring may predict outcome in pediatric IBD (PIBD)

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Background and objectives: There are no data on therapeutic drug monitoring (TDM) of vedolizumab in children. We aimed to 1) explore repeated TDM in children receiving vedolizumab; 2) associate drug levels with disease outcome; 3) to compare two different commercial assays.

Methods: 33 serum samples were measured on 12 children (42% Crohn's disease, 33% IBD-U and 25% UC, all previously failed anti-TNF; mean age 15.6±1.4 (range 13-18yrs), disease duration 4.4 (IQR 0.88-5.3) years). All patients received 300mg vedolizumab induction infusions at weeks 0, 2 and 6. Serum samples were obtained at weeks 2, 6, and 14 and were measured using two different ELISA kits: LISA TRACKER (Theradiag, France) and IDKmonitor (Immundiagnostik AG, Germany). Four patients had also week 30 samples.

Results: The median vedolizumab levels were 41.6µg/ml (IQR 33-51), 23µg/ml (16-32), 5.5µg/ml (0.8-9.4) and 8.4µg/ml (4.9-25) at weeks 2, 6, 14 and 30, respectively (Figure 1). The agreement of both kits was excellent with Intraclass correlation coefficient (ICC)=0.97 (95%CI 0.86-0.99) at week 6 and 14. All had levels >3µg/ml at weeks 2 and 6. At week 14 two patients had undetectable levels; in one the infusions intervals had been shortened to q4wks and her levels at week 30 were 8µg/ml while entering clinical remission. Both kits agreed in all cases of levels<3. Week 2 TDM did not predict outcomes at week 14. While week 6 TDM did not predict clinical remission at week 14 (i.e. PUCAI or wPCDAI<10), it was highly associated with CRP values in the 7 children with available measures (Figure 2).

Conclusions: The reliability of TDM monitoring of vedolizumab in pediatric IBD is high as reflected by excellent inter-sampling of two different kits. Vedolizumab TDM seems important in detecting children who require escalated dosing and in predicting short term CRP values, but a larger study is required.

EP40. Subcutaneous ustekinumab provided clinical and biological benefit for 9/12 refractory pediatric Crohn's disease

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Objectives and study: Ustekinumab has shown a good safety profile and efficacy to induce and maintain remission in adult patients with refractory Crohn's Disease (CD). Data are lacking in children.

Methods: All CD patients under 18 years who received ustekinumab were included in this retrospective observational study performed in a single tertiary pediatric centre.
Results: From January 2015 to May 2016, twelve CD patients were treated with ustekinumab, all because of failure of several lines of therapies including anti-TNF antibodies. All but one patient were followed at least one year. An initial response was achieved in 9 (75%) patients, and remission in 5 (42%). At one year, the nine responders were still receiving ustekinumab with clinical benefit and without steroids need. Seven of them (58%) were on clinical remission. One patient experienced a serious adverse event and the treatment was stopped after the first injection.

Conclusion: Subcutaneous ustekinumab is effective to induce and maintain remission in severe pediatric CD refractory to anti-TNF antibodies.

Key words: Pediatric, Crohn's disease, anti-TNF-α, therapeutics.

HARD POSTERS

P001. Genetic and serological profile as markers of disease susceptibility in siblings of children with inflammatory bowel disease

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Introduction: Having a family history for IBD is the only known risk factor for disease development. Recent data have shown that genetic and serological markers may predict IBD development. However, only few studies evaluated a genetically well-characterized population and at high risk for disease, such as siblings and twins.

Aims: Aim of this study was to evaluate genetic and serological markers of disease susceptibility in healthy siblings and twins of children with IBD.

Materials and methods: This is the first phase of a prospective, longitudinal, multicenter, case-control study. Serum was collected from 80 siblings and twins of children with CD and 77 healthy controls with no family history for IBD. Genotyping (TaqmanMGB) for variants of ATG16L1 (SNP rs2241880), STAT3 (SNP rs744166), ECM1 (SNP rs3737240), NKKX2-3 (SNP rs10883365), was performed. Serological titers of anti-Saccharomyces cerevisiae (ASCA IgG and ASCA IgA), perinuclear anti-neutrophil cytoplasmic antibodies (pANCA), anti-outer membrane porin C antibody (anti-OmpC), and antibacterial flagellin antibody (anti-CBir1), were determined by specific enzyme-linked immunosorbent assay (ELISA).

Results: Fifty-nine out of 80 cases (74%) and 50/77 controls (65%) were positive for at least 1 of the serum autoantibodies (p=0.29); a combination of any 4 of them was found in 3 cases (4%) and no controls (p=0.28). No significant difference was shown for any of the studied autoantibodies between cases and controls. Homozigosity for any susceptibility gene variant was found in 60 out of 80 cases (75%) and in 52/77 controls (67.5%) (p=0.37), with no significant association between family history and genotype status. No combination of gene variants significantly differed between cases and controls.

Conclusions: Our preliminary results argue against a role of commonly recognized genetic polymorphisms and microbial antibodies as markers of disease susceptibility in siblings of children with IBD. However, data from larger and prospective studies are warranted before drawing definite conclusions.

P002. Role of microrna-223 in the activation of poly(aden-ribose) polymerase in pediatric patients with Crohn's disease

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Background: Crohn's disease (CD) is a multifactorial disease, characterized by oxidant-induced tissue injury with a possible activation of the poly(ADP-ribose) polymerase (PARP-1). However, there are no studies examining PARP activation in patients suffering from CD. MicroRNAs (miRs) can offer a potential missing link between the genetic susceptibility, environmental and immunologic factors involved in the pathogenesis of CD. Previously PARP-1 was identified as a direct target gene of miR-223 in an epithelial cell line.

Aims: to examine the level of PARP activation and the expression of miR-223 in colonic biopsies of pediatric CD; to study the role of inflammatory processes, the effect of lipopolysaccharide (LPS) on PARP activation and miR-223 expression is examined in HT-29 colonic epithelial cell line.

Methods: Colonic biopsies were taken from patients with macroscopically inflamed and intact mucosa with CD and controls. LPS treated HT-29 cells serve as our in vitro model. To analyze PARP activation western blot analysis (antibody against the enzyme and the end product of PARP activation: poly(ADP-ribose) (PAR)), immunohistochemical, immunofluorescent labeling and RT-PCR were used. To analyze the expression of miR-223 RT-PCR was used.

Results: PARP-1 and miR-223 expression was elevated, however the amount of PARP and PAR was reduced in pediatric CD compared to the controls. The LPS incubation did not affect the expression of PARP-1 mRNA, however decreased the expression of miR-223, and enhanced PARP activation.

Discussion: In our study we showed that the expression of miR-223 is up-regulated and PARP activation is reduced in pediatric patients with CD. Moreover, we confirmed the opposite change in vitro, too. These data suggest that the hypofunctionality of PARP may play a potential role in the pathomechanism of CD.

"SUPPORTED BY THE ÚNKP-16-3-Ill NEW NATIONAL EXCELLENCE PROGRAM OF THE MINISTRY OF HUMAN CAPACITIES"

Gábor Veres and Eszter M. Horváth equally contributed to this work.
Introduction: Early nutrition can influence the clinical course of inflammatory bowel disease through the microbiome.

Aim: Study the relationship between breastfeeding (BF) and the clinical severity of Crohn's disease (CD) in childhood.

Methods: Data from CD patients under 18 years old was retrieved retrospectively from medical records. Disease severity was defined as the need for surgical intervention due to CD-related complications. Patients were labeled as cases or controls according to it. Exposure to human milk was considered positive if BF lasted more than 4 months. This was recorded after telephone interview. The possible confounding effect of several CD features was studied. Controls were selected on matching by frequency based in the characteristics that behaved as confounders. Odds ratio (OR), and its 95% confidence interval (95%CI), was calculated by multivariate logistic regression, with adjustment for matching covariates. Finally, a stratified analysis was also conducted to assess the interaction between BF and other factors influencing CD severity.

Results: Among the 133 CD patients included, 23 had surgery performed. Follow up period ranged between 2 and 17 years. Four confounders were identified: upper digestive system involvement, isolated ileal disease (ILD), perianal affection and nonstenotic/nonfistulizing (or inflammatory) pattern. Adjusted effect of BF over CD severity reached an OR = 0.36 (95%CI 0.10 to 1.27) with a p-value = 0.112. Inflammatory pattern (OR = 0.08) and isolated ileal involvement (OR = 4.53) significantly influenced the risk of surgery. BF increased the protective effect of the inflammatory pattern (OR change from 0.17 to 0.05) and decreased the effect of ILD (OR change from 6.50 to 3.47). However the interaction did not reach statistical significance.

Conclusions: BF has not an independent early nutrition programming effect on the severity of CD. Nevertheless, it shows a tendency to favourably modulate the impact of truly risk factors for surgery.

P005. Presence of eosinophil cells in the lower gastrointestinal tract of healthy children - a meta-analysis

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Background and aims: Eosinophil infiltration of various tissues is present under physiological conditions. In primer eosinophil cell associated gastrointestinal diseases, there are no detectable ethiologic factor behind the increase of cell counts. In the case of the lower gastrointestinal tract (GI) there is no consensus on the normal levels of tissue eosinophil cell counts. Publications vary highly in the value of empiric criteria 6-50 eosinophil cell/High Power Field (HPF). The aim of the current study was to review the available sources regarding healthy tissue specimen originating from lower GI fractions, to assess the validity of suggested diagnostic cut-offs.

Data sources and methods: Pubmed, Scopus and Cochrane and EMBASE databases were screened. 27 publications were systematically screened for eligible numeric data. 10 publications were enrolled in a quantitative meta-analysis.

Results: In the small intestine the overall cumulative mean cell number was 9.44 (95% CI: 5.17, 13.71), with an estimated prediction interval (PI) of 0-24.96. For the large intestine and the rectum the overall cumulative mean cell number was 11.10 (95% CI: 9.11, 13.09) with estimated PI of 0.96-21.23. Heterogeneity of data was significantly high, and more than 50% of the data sources were incomparable due to inappropriate data reporting.

Conclusions: The upper limits of the overall predictive intervals for the small and the large intestine were congruent with the generally used criteria for pathologic tissue eosinophil numbers. However, this limits are not confident, the data show a large amount of heterogeneity. Considering the relatively small number of
appropriate data sources, the validity of the predictive interval as a base for diagnostic cut-off is not supported. Therefore, the objective diagnosis of eosinophilic enteritis and colitis is not possible. Conducting prospective examinations, with adherence to an established endoscopic and histological evaluation protocol is needed to provide high level evidence for the diagnostic procedures.

**P006. Faecal microbiota dysbiosis in Pediatric inflammatory bowel disease worsens after therapy.**

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Introduction: Imbalances in the faecal microbiota with a reduction in biodiversity; dysbiosis, have been reported in inflammatory bowel disease (IBD).

Aims: Our aim was to characterize the faecal microbiota in paediatric patients with newly diagnosed untreated IBD and to study microbiota changes in IBD patients one year after treatment.

Material and methods: Faecal samples were collected from 235 children < 18 years of age. IBD was diagnosed in 110 patients (80 Crohn’s disease (CD), 27 ulcerative colitis (UC), 3 IBD unclassified). Fifty patients had gastrointestinal symptoms but no IBD; non-IBD symptomatic patients, and 75 were healthy children. Of the IBD patients, 31 (9 UC and 22 CD) had repeated faecal microbiota analysis one year after therapy, 16 (52%) of these had been treated with infliximab. The microbiota was analysed at baseline and after treatment using a 16S rRNA DNA based test with the GA-map technology, measuring probe signal intensity (PSI) of 54 DNA probes targeting 300 bacteria.

Results: At baseline most bacterial PSIs were reduced in IBD and non-IBD patients (both p<0.001) compared to healthy controls. IBD patients had reduced abundance of Eubacterium spp. (p<0.01), Parabacteroidetes and Bifidobacterium (both p=0.02) compared to non-IBD patients.

After therapy the microbiota was even more dysbiotic than at baseline, regardless of IBD type, disease activity and treatment modality, with less abundance of Dorea, Lachnospiraceae and Eubacterium hallii (p<0.001). Compared to healthy and non-IBD patients the microbiota composition after treatment had less abundance (p<0.001) of Akkermansia muciniphila, Bacteroides, Prevotella and Veillonella besides higher abundance of Streptococcus sanguinis, Atopobium rimae and Proteobacteria.

Conclusions: The faecal microbiota composition is different in paediatric IBD and non-IBD symptomatic patients compared to healthy children. A severe dysbiotic microbiota profile seems to persist and worsen after treatment in paediatric IBD patients regardless of IBD type, disease activity and treatment modality.

**P007. Prognostic Value Of Probe-Based Confocal Laser Endomicroscopy In Pediatric Inflammatory Bowel Diseases**

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Background and objectives: The incidence of inflammatory bowel diseases (IBD), including Crohn disease (CD) and ulcerative colitis (UC), is increasing in children. We recently demonstrated increased epithelial gaps in the duodenum of IBD patients, and high capillary flow rates in the duodenum of UC patients using probe-based confocal laser endomicroscopy (pCLE). In this study, we aimed to analyze if increased epithelial gap density or capillary flow could predict the clinical course of IBD patients.

Methods: A total of 26 IBD patients (16 CD and 10 UC cases) for the epithelial gap study, and 9 UC patients for the vascular flow study were used to determine differences between the groups. Cox proportional hazard models were used to determine if gap density or vascular flow were predictors of risk of clinical events or inflammatory parameters.

Results: Patients were followed for a mean of 31 months (range 12-45). While high epithelial gaps and high capillary flow rates did not predict the risk of clinical events in IBD patients, CD patients with high epithelial gaps (but not those with normal gaps) who were treated with infliximab had a significant reduction in ESR at the 12-month follow-up time point.

Conclusions: We show a correlation between high epithelial gaps in the non-inflamed duodenum in CD patients and a drop in ESR in patients treated with infliximab. Future studies evaluating epithelial gaps and capillary flow in pediatric IBD patients and their relation with inflammatory parameters and infliximab might be helpful in better selecting treatments for patients.

Key words: IBD, pCLE, ESR

**P008. 2016: the epidemic of inflammatory bowel disease.**

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Introduction: An epidemic is the appearance of a particular disease in a larger than expected number of people at a certain time and location. Asturias is a 1.000.000 inhabitants region in the North of Spain. In this region, until 2015 2 new cases of Inflammatory Bowel Disease (IBD) were diagnosed every year. In 2016, 15 new cases were diagnosed.

Aims: Epidemiological, clinical and other features are described and compared with previous years.
Background and objectives: There is no nation-wide, long-term follow-up epidemiological study in pediatric inflammatory bowel disease (pIBD), especially in the era of biologicals. The Hungarian Pediatric IBD Registry (HUPIR) is a nation-wide, prospective registry. We analyzed the follow-up data of the pIBD cases diagnosed in 2010 in HUPIR.

Methods: Newly diagnosed pIBD patients (ages 0–18 years) are registered in this prospective, nation-wide registry (HUPIR), and followed-up yearly. The questionnaire includes epidemiological data, localization, disease activity indexes and initial therapy. At follow-up, frequency of relapses, therapy, activity are recorded. Descriptive statistical methods and Kaplan-Meier analyses were applied.

Results: Between 1st January 2007 and 31st December 2014, 1168 IBD cases were identified. Incidence of IBD increased from 7.1/100000 to 9.1/100000 during 8 years.

Conclusions: The incidence of pIBD has increased in the last years in Hungary. The follow-up of pIBD cases is difficult due to transition to adult health care. The disease course was similar to other cohorts.

Keywords: epidemiology, follow-up, incidence

P010. Diagnostic Delay in Pediatric Inflammatory Bowel Disease in Spain: The SPIDER Registry

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Introduction: Diagnostic delay (DD) in Inflammatory Bowel Disease (IBD) has important clinical impact. There is increasing evidence showing a higher success rate when treatment is administered early in the disease.

Aims: To evaluate DD in paediatric IBD in Spain.

Material and Methods: Multicentric prospective observational study including paediatric IBD patients diagnosed during two consecutive years in 24 paediatric centers. Information was obtained from a questionnaire filled in by the treating paediatric gastroenterologist. Data were analyzed with the program SPSS 18.

Results: Data from 149 patients (59.7% males) were obtained. Mean age at diagnosis was 11.41 years (SD 3.0). Disease distribution: Crohn’s disease (CD) 95 patients (63.8%), ulcerative colitis (UC) 50(33.6%), IBD unclassified (IBDU) 4 (2.7%). Median DD was 19.14 weeks (IQR 33.14), being significantly longer (p=0.001) in CD (27.5 w, IQR 38.93) than in UC (13.7 w; IQR 18.54). Family IBD history was not associated with shorter DD. Median time from appearance of symptoms to consultation with the first physician involved in the process was 2 weeks (IQR 3.64), from this first visit to being sent to the paediatric gastroenterologist (PG) 7 weeks (IQR 19.29); from referral to the PG visit 1 week (IQR 4.14), and from this visit to the diagnosis 1.7 weeks (IQR 3.57). There was a significant negative correlation in UC patients between the PUCAI score and DD (-0.3; p=0.04). The median of physicians visited before the PG was 2 (IQR 2), and 32.7 of patients consulted the same physician more than 4 times.
Conclusion: DD in CD was significantly longer as compared to UC. The major component responsible for DD in IBD was the time spent between the FPC and the PG referral. A significantly negative correlation was found between the PUCAI score and DD in UC patients.

P011. Development and Validation of Diagnostic Criteria for IBD Subtypes Including IBD-unclassified in Children

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Introduction: The revised Porto criteria identify subtypes of paediatric inflammatory bowel diseases: ulcerative colitis [UC], atypical UC, inflammatory bowel disease unclassified [IBDU], and Crohn’s disease [CD].

Aims: In continuation of the Porto criteria, we aimed to derive and validate criteria, termed “PIBD-classes”, for standardizing the classification of the different IBD subtypes.

Materials and Methods: This was a multicentre retrospective longitudinal study from 23 centres affiliated with the Port -group of ESPGHAN. Both a hypothesis-driven judgmental approach and mathematical classification and regression tree [CART] modeling were used for creating a diagnostic algorithm. Since small bowel inflammation is easily recognized as CD, we focused here primarily on the phenotype of colitis.

Results: Among all, 749 IBD children were enrolled: 236 [32%] Crohn’s colitis, 272 [36%] UC and 241 [32%] IBDU [age 10.9 ± 3.6 years] with a median follow up of 2.8 years (interquartile range [IQR] 1.7–4.3). A total of 23 features were clustered in three classes according to their prevalence in UC: six class-1 features [0% prevalence in UC], 12 class-2 features [≤5% prevalence], and five class-3 features [5–10% prevalence].

According to the algorithm, the disease should be classified as UC if no features exist in any of the classes. When at least one feature exists, different combinations classify the disease into atypical UC, IBDU or CD. The algorithm differentiated UC from CD and IBDU with 80% sensitivity (95% confidence interval [CI] 71–88%) and 84% specificity [77–89%], and CD from IBDU and UC with 78% sensitivity [67–87%] and 94% specificity [89–97%].

Conclusions: The validated PIBD-classes algorithm (figure 1) can adequately classify children with IBD into small bowel CD, colonic CD, IBDU, atypical UC, and UC.

P012. Preliminary study of atypical ulcerative colitis and inflammatory bowel disease unclassified in korean pediatric onset IBD

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Introduction: The prevalence of atypical ulcerative colitis (UC) and inflammatory bowel disease unclassified (IBDU) in pediatric-onset IBD (PIBD) has been increased in Korea. The revised Porto criteria was proposed to standardize the PIBD subtypes and provide a clear definition of atypical UC and IBDU which used to be subjective.

Aims: This study aims to evaluate a change of diagnosis from originally diagnosed UC to atypical UC and IBDU respectively in Korea by using the revised Porto criteria.

Material and methods: We retrospectively reviewed the medical record of 135 UC who had been diagnosed before the age of 18 by PIBD experts according to the accepted diagnostic criteria at the time of diagnosis from 2005 to 2013. Each data was categorized by its baseline and follow-up disease characteristics based on endoscopic and histologic findings.

Results: Among total of 135 patients, 48 UC patient data were eligible to evaluate the change of diagnosis based on the Porto criteria. While 20/48 (41.7%) of UC children maintained their original diagnosis, 28/48 (58.3%) of UC patients were reclassified to atypical UC and none of the patients changed to Crohn’s disease (CD).
Conclusions: The Porto criteria suggested that the prevalence of atypical UC could be greater than that of CD among those who had been previously diagnosed as pediatric UC in Korea. Given the notion of atypical UC and IBDU as a true intermediate phenotype of PIBD, clinicians should consider multiple variables of the criteria and undergo complete endoscopic and histologic work-up at the time of diagnosis with repeated investigation for every PIBD patient.

Keywords: Korean pediatric inflammatory bowel disease, atypical ulcerative colitis, revised Porto criteria


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Background and Objectives: Mitsuyama et al. reported antibodies to Crohn’s disease (CD) peptide 353 (ACP353) as a novel serologic marker for diagnosis of CD in adults (Clin Exp Immunol 2011 and J Gastroenterol 2014). In the CD patients, ACP353 had a higher sensitivity and specificity (63% and 91%, respectively) than anti-Saccharomyces cerevisiae antibodies, ASCA (47% and 90%). We aimed to clarify whether ACP353 is useful for diagnosis of CD in children.

Methods: In a single-center study using enzyme-linked immunosorbent assay, serum ACP353 levels were determined in 10 patients with CD, 26 with ulcerative colitis (UC), 4 with other intestinal diseases, and 11 healthy controls. All subjects were under 17 years old. We set cut-off value for positivity at 2.94 U/ml for ACP353. We compared sensitivity for diagnosis of CD in 5 early-onset CD patients (EOCD, under 10 years old) with those in 5 late-onset CD (LOCD, 10-16 years old).

Results: ACP353 levels were elevated in CD patients (median, 7.12 U/ml) than UC (0.64 U/ml; P=0.08), the other intestinal diseases (0.61 U/ml; P=0.14), and healthy controls (0.58 U/ml; P=0.01). The sensitivity and specificity for diagnosis of CD were 50% and 98%, respectively. The sensitivities for diagnosis of CD in EOCD and LOCD were 20% and 80%, respectively.

Conclusions: ACP353 may be a useful serologic marker for diagnosis of pediatric CD, particularly, LOCD. Further investigation is ongoing as a multicenter prospective study in Japan.

Keywords: antibodies to Crohn’s disease peptide 353 (ACP353), serologic marker, diagnosis of Crohn’s disease, sensitivity, specificity

P014. Fecal calprotectin as a reliable marker for differentiating inflammatory bowel disease from food allergy and functional abdominal pain in children

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Aims: Fecal calprotectin (FCal) is used as a noninvasive marker to rule out inflammatory bowel disease (IBD) in children with chronic gastrointestinal symptoms. We aimed to evaluate diagnostic accuracy of FCal for gastrointestinal inflammation and optimal cutoffs to differentiate IBD from eosinophilic gastroenteritis (EoGE) and functional abdominal pain disorders (FAPD) in children with chronic gastrointestinal symptoms.

Method: Between August 2015 and March 2017, a total of 253 children (123 boys and 130 girls, aged 2.9-17.8 years) were recruited and divided into the 3 study groups; FAPD (n=187), IBD (n=38), and EoGE (n=26). FCal, WBC, ANC, ESR, and hsCRP were measured at initial diagnosis in all subjects. Spearman correlation analysis was performed to evaluate the correlation between FCal and other inflammatory markers. Receiver-operating characteristics plot analysis was used to evaluate optimal cutoff levels of FCal.

Results: Median FCal levels of FAPD, EoGE, and IBD in pediatric patients were 23.4 (11.5-1285.5) µg/g, 77.5 (11.5-2000) µg/g, and 2000.0 (60.4-20000) µg/g, respectively, which were significantly different among the 3 groups (p < 0.001). In the IBD group, FCal positively correlated with ESR (r = 0.569, p < 0.001) and hsCRP (r = 0.480, p = 0.004). In the EoGE group, FCal positively correlated with ESR (r = 0.566, p = 0.004). A cutoff of FCal 292.7 µg/g distinguished IBD from FAPD with a sensitivity of 92 % and a specificity of 95 %. A cutoff of FCal 677.4 µg/g distinguished IBD from EoGE with a sensitivity of 81 % and a specificity of 89 %. Conclusion: FCal measurement is a useful and reliable noninvasive marker in differentiating pediatric IBD from other gastrointestinal diseases, such as food allergy or FAPD in children manifesting with chronic gastrointestinal symptoms, when optimal cutoffs are applied.

P015. Fecal metalloproteinase-9 and serum tissue inhibitor of metalloproteinase-1 discriminate children with Crohn’s disease

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Introduction The diagnosis of Crohn’s disease (CD) and proper classification of disease activity is usually challenging and requires invasive tests, like colonoscopy. Aims The aim of study was to determine the usefulness of new non-invasive markers representing gut mucosal damage (Metalloproteinase-9, MMP-9) and remodeling (tissue inhibitor of metalloproteinase-1, TIMP-1), gut wall fibrosis (Galectin-3) in diagnosis, and severity assessment of CD in children. Material and methods Serum and fecal MMP-9, TIMP-1 and Galectin-3 concentrations were measured with ELISA in 26 children with CD and 21 controls. Disease activity was determined with pediatric Crohn’s disease activity index (PCDAI). Based on Spearman analysis the correlations between each marker and serum CRP, ESR, CBC, albumin, endoscopic activity and PCDAI were tested. The cut-off levels, specificity and sensitivity were calculated using receiver operating characteristic (ROC) analysis.

Results CD children demonstrated significantly higher levels of serum MMP-9, TIMP-1 and fecal MMP-9, TIMP-1 compared to controls (all p<0.05). Among fecal markers the best discriminators for CD patients were MMP-9, with the area under curve (AUC) of 0.963 (95%CI 0.884 to 1) for MMP-9, followed by TIMP-1 with AUC of 0.943 (95%CI 0.774 to 1). The best serum marker for CD group was TIMP-1 with AUC of 0.943 (95%CI, 0.853 to 1), followed by MMP-9 with AUC of 0.85 (95%CI, 0.677 to 1) and Galectin-3 with AUC of 0.718 (95%CI, 0.474 to 0.963) compared to controls. No association between tested markers and clinical and endoscopic activity index, and CRP or ESR was found in CD group. However, the serum level of TIMP-1 inversely correlated with albumins and MPV (p<0.05), the known inflammatory indicators.

Vol. 65, Supplement 1, October 2017
Conclusion The increased level of serum MMP-9, TIMP-1 and fecal MMP-9, TIMP-1 differentiated children with CD from controls. Further studies to evaluate the usefulness of these markers are required for larger group of CD patients.

P016. Fungal dysbiosis in mucosa and stool: accuracy in predicting diagnosis of Crohn’s disease in children

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Introduction: Bacterial dysbiosis has been reported as potential screening method for CD with more accurate mucosal than fecal samples. Although fungal dysbiosis has been demonstrated in adults and children with CD, the accuracy in predicting CD has not been reported. Aim: to assess the performance of fungal mucosal and fecal dysbiosis in predicting CD in a cohort of newly-diagnosed children with Crohn disease.

Material and methods: Mucosal and fecal samples were collected from children with CD and controls (51 samples from CD and 24 from controls). Fungal community structure was determined using 454 pyrosequencing of bar-coded 16S rRNA genes. Abundance and diversity of fungal taxa in mucosa and stool were compared. Sparse logistic regression was used to predict the diagnosis of CD based on fungal microbiota. The accuracy of the classifier was tested by computing the receiver operating characteristics (ROC) curve with 5-fold stratified cross validation under 100 permutations of the training data partition. Only results with q value below 0.05 were considered significant. Results: The mean age was 13.9 years for CD children and controls. At diagnosis, CD location were L1 in 4 and L3 in 12 children while CD behavior was B1 in 13 and B2 in 3 children. In these patients, except for Saccharomyces cerevisiae (S. cerevisiae) and bayanus which were significantly more abundant in stool (p=0.02 and p=0.003 respectively), the significantly lower abundance of most fungal species and reduced fungal diversity in stools than in mucosa suggest that stools are more dysbiotic in CD. The mean area under the ROC curve (AUC) was significantly higher in stools (AUC= 0.85 ± 0.057) than the mucosa (AUC= 0.71 ± 0.067) (p=2.8.10^{-17}). Conclusions: Unlike bacterial dysbiosis, we find higher accuracy of fungal fecal than mucosal dysbiosis in predicting CD, indicating another potential non-invasive screening test for CD in children.

P017. Small bowel capsule endoscopy examinations for detecting small intestinal lesions of Crohn’s disease in children – a 7 years experience

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Introduction: The main indication for video capsule endoscopy (VCE) in children is the assessment of small bowel Crohn’s disease (CD). VCE provides a high diagnostic yield comparable to magnetic resonance-based enterography or enteroclysis, and has a high sensitivity in detection of early and proximal small intestinal lesions of CD.

The aim of our study was to assess the diagnostic value and tolerance of VCE in paediatric patients with inflammatory bowel disease (IBD). Methods: This is a retrospective review of the VCE studies (n:106, PillCam SB, Given Imaging) that were performed in our institution from January 2010 to March 2017. Results: Indications for the procedure in 70 cases were confirmed or suspected CD (n:16), ulcerative colitis (UC) n:14, undeterminate colitis (IBDu) n:8, suspected CD n:32), 54% of them were males, median age was 11.5 years (range: 3.0 to 18.0). In 8 cases the VCE was placed endoscopically into the duodenum under general anaesthesia. In 79% of the cases the VCE was seen in the coecum at the end of recording (9-12 hours) with a median small bowel transit time 273 minutes (range 87 to 551). Three of children retained the capsule, only one needing surgical removal of terminal ileum stricture. Positive findings were observed in 45/70 (64%), of which 31% were helpful in terms establishing a new diagnosis, and in 69% of cases there were changes in the therapeutic approach of the patient. We found no correlation between Crohn’s disease activity index (PCDAI) and CE activity score (Lewis score).

Conclusions: Our experience demonstrates that VCE is a useful and safe diagnostic modality in childhood inflammatory bowel disease.

P018. Wireless capsule endoscopy: exploring the bowel in pediatric IBD patients

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BACKGROUND AND OBJECTIVES: Conventional endoscopy presents limitations for inflammatory bowel disease (IBD) diagnosis in children. Wireless capsule endoscopy (CE) allows exploring the entire small bowel (SB). The objective is to provide our experience with CE in pediatric patients with IBD.

METHOD: PillCam Wireless capsule® was administered by mouth or placed by endoscopy. After eight hours registry, images were displayed on the workstation.

RESULTS: 45 patients with suspected IBD (4-15 years) have been studied; they have previously undergone gastroscopy, colonoscopy, magnetic resonance enterography, small bowel follow-through series, ultrasound and or nuclear medicine.IBD was ruled out in 11 cases and 42 examinations were performed in 34 children with a final diagnosis of IBD. In 7 cases the CE was crucial to reach Crohn’s disease diagnosis (CD), in 20 with CD it was used for extension study and in six out of these 20 cases, remission and or relapse were also evaluated. In 7 patients with histological diagnosis of IBDU CE was performed to assess small bowel involvement.

COMMENTS: CE is a suitable technique for exploring SB. CE allows discarding IBD. It is striking the presence of lesions throughout the digestive tract, even in proximal areas, in all our patients with Crohn’s disease.

CE is well tolerated in children older than 4 years. CE is extremely useful in selected cases for diagnostic purposes as well as for extension and evolutionary control studies, even in small patients.

KEY WORDS: Wireless capsule endoscopy, diagnosis , small bowel
P019. Inflammatory bowel disease – “Reclassified”

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Background: The diagnosis and classification of Inflammatory Bowel Disease (IBD) can be difficult. In some cases, it may be impossible to classify cases as Crohn’s Disease or Ulcerative Colitis, calling them IBD-Unclassified (IBD-U). It is still unclear whether this subtype is a specific entity or an IBD that will evolve and be reclassified over time. The use of a validated algorithm may facilitate the classification of the ambiguous cases.

Aims: To characterize a pediatric population diagnosed with IBD-U by applying the revised diagnostic criteria of the IBD Porto Group of ESPGHAN.

Methods: This was a descriptive and analytical retrospective study, with analysis of the variables: gender, clinical, endoscopic and histological presentation, radiographic and serological parameters, and evolution.

Results: Nine children were identified, 56% female, with a mean age of 11 ± 3.6 years at diagnosis. In 78% symptoms were suggestive of Ulcerative Colitis; 22% had abdominal pain and constitutional symptoms. There was a family history of IBD in 1/3. Diagnosis was established 4 months (1-24) after the onset of symptoms. Currently, after a 1.4-year follow-up period (0.25-4.75), 8 patients are in clinical and analytical remission (56% on oral plus/or topical mesalazine, 44% mesalazine plus azathioprine), 1 with active disease due to non-compliance. After applying the diagnostic algorithm, it was possible to reclassify 6 of the 9 cases (67%; 2 cases reclassified as Crohn’s Disease and 4 as Ulcerative Colitis). One of the patients with IBD that was not “re-classifiable” in the initial investigation was reclassified 3 years later as Ulcerative Colitis.

Conclusion: The application of the new criteria is useful in the diagnostic classification of a significant percentage of patients by using a systematic re-evaluation of all features. However, some cases may persist unclassified and the definitive diagnosis may depend on the longer evolution.

P020. A single centre study comparing USS small bowel and MRI enteroclysis in early onset Crohn’s disease

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Introduction: Small bowel imaging part of the diagnostic work up in early onset IBD. The utility of Ultrasound abdomen (USS) in small bowel disease has been poorly evaluated in early onset IBD.

Aims and objectives: We aimed to evaluate the adequacy of USS in detecting the presence of small bowel disease at the initial work up of early onset IBD according to the Porto Criteria.

Materials and Methods: Data from patients with an established diagnosis of Crohn’s disease that had MRI small bowel as part of disease reassessment during a three-year period (2013-2015) was collected. Usual practice at our centre is for all patients to have an USS small bowel at the initial presentation; unless surgical complications are suspected. Findings on MRI performed during disease were compared with historical USS data at the beginning of illness or to an USS done concurrently for disease location, behaviour, and presence/absence of complications.

Results: Forty-seven patients with MRI small bowel study were eligible. The median age at initial diagnosis was 11.2 years. All had USS small bowel at the time of diagnosis. Nineteen/25 patients had abnormalities on MRI small bowel that were previously found on the initial diagnostic ultrasound. 5/25 of patients who had normal initial ultrasound had MRI abnormalities either indicative of small bowel disease progression or the limitation of USS small bowel. Of the 47 patients who had MRI small bowel as part of disease reassessment, 11 patients had a preceding ultrasound within 3 months. The concurrent USS was abnormal in 8 patients. 2 patients with USS abnormalities had in fact a normal MRI and 8 were abnormal.

Conclusion: USS small bowel in the hands of a trained paediatric radiologist is useful in detecting small bowel disease. These changes accurately predict changes seen on MRI.


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Introduction: Clinical and imaging differences of IBD are known among children and adults, but in Latin America we do not have an imaging parameter to guide us.

Objective: Is to describe these differences in a population of Colombian children. Methods: We analyze 31 imaging-based of 22 to 35 patients younger than 18 years, diagnosed with IBD: Crohn’s (EC) or Ulcerative Colitis (UC) were analyzed with Ultrasound (US), CT scan, and Magnetic Resonance (MR) in a Pediatric Hospital between 2001 and 2016. Results: The mean age was 12, (2 to 17 years). The sex distribution was similar: Seven girls from 14 cases of CD and 11 from 21 cases from UC. The most common clinical finding was the thickening of the colon wall at 81% for each entity; enhancement of the colon wall in 63% with CD and 27% in UC; prominence of the vasa recta in 54% with CD and 63% with UC; mesenteric fat stranding in 54% of CD and 36% of UC; alteration of colon wall stratification in 27% with CD and 18% with UC. The compromise of the ileocecal valve, the presence of fistulas in 18% and stenosis in 9% were found for CD only. Hyperemia of the wall, seen with Doppler, and an increase in size of lymph nodes (5 to 10 mm) was observed in 18% of cases for both CD and UC. Pseudopolyps: in 18%, only with UC. In none of the cases was compromise of the small bowel observed. Conclusions. Since we did not find a history of imaging studies in children in Latin America, this work not only shows differences with the changes observed in adults, but also serves as a parameter for a reasonable complementation and interpretation of data and findings in our region.
P022. Inflammatory bowel disease in children is a challenging diagnosis when overlaps with coeliac disease

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Background. IBD and coeliac disease (CD) are conditions which can overlap in paediatric patients although this is uncommon and difficult to confirm. Aim. We present our experience with patients who developed both conditions during early years of life. Methods. We retrospectively reviewed all IBD patients seen in our centre who also had a diagnosis of coeliac disease over a 10-year-period. Data were collected from electronic notes. Demographics, consultations, laboratory and endoscopic findings were extracted for descriptive analysis. Results. 8/578 patients were found to have both diagnosis, this accounts for 1.4% of all paediatric IBD patients seen in our centre (mean 57 new patients per year, past 10 years). 5/8 were female, 1 male had Down syndrome, 1 patient had incomplete records. Mean age of diagnosis was 7.1 and 8.9 years for CD and IBD respectively. 4/8 patients suffered of Crohn's disease, 3/8 of ulcerative colitis and 1/8 of IBD unclassified. 3 patients were diagnosed with both entities within 3 months, other 4 had a previous history of CD and developed IBD years later (mean 3.0 years). 4/7 patients had positive anti-transglutaminase serology. Endoscopic findings were difficult to interpret; complementary immunostaining, small bowel imaging and video capsule endoscopy were required in order to support both diagnoses. Endoscopic assessment for known 4 CD patients obeyed to persistent gastrointestinal symptoms, features included granulomata and cryptitis in small bowel (3/4) and pancolitis (1/4). Conclusion. IBD can overlap with CD in paediatric patients although this association is rare. IBD can follow the appearance of CD years later and can also present at the same time of CD. Proving the coexistence of IBD and CD in children is a challenge, and requires of a multidisciplinary team. IBD must be considered in CD patients when symptoms do not seem to respond to a gluten-free diet.

P023. Laboratory values in japanese children with newly diagnosed inflammatory bowel disease: a single-center experience

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Background and Objectives: Laboratory values in children with newly diagnosed IBD have been reported from Europe and North America but not Asia. We aimed to clarify laboratory values in Japanese children with newly diagnosed IBD. Methods: We retrospectively reviewed patients under 16 years old who were newly diagnosed with ulcerative colitis (UC) or Crohn’s disease (CD) at Kurume University Hospital between 2008 and 2015. Clinical and laboratory findings at time of diagnosis were recorded. We also reviewed children diagnosed with irritable bowel disease who had normal lower endoscopic findings as controls. Disease activity was determined using the Pediatric Ulcerative Colitis Activity Index (PUCAI) or the Pediatric Crohn’s Disease Activity Index (PCDAI). We evaluated hemoglobin (Hb), platelet count (Plt), albumin (Alb), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), and compared the values in our IBD patients with those in controls and in Western reports. Results: Subjects with UC and CD numbered 31 and 15, respectively. Percentages of normal values of Hb, Plt, Alb, CRP, and ESR in UC/CD were 45/47, 68/53, 84/40, 81/7, and 35/0 %, respectively. Plt and CRP in UC did not differ significantly from values in controls. Alb and ESR were significantly different between UC and CD in both mild and moderate-severe groups. In patients with onset before age 10 years, values in UC did not differ significantly from CD. In UC, ESR correlated positively, while Hb and Alb correlated negatively, with PUCAI. In CD, CRP and ESR correlated positively with PCDAI. Conclusions: Percentages of Japanese children with IBD showing normal laboratory values at time of diagnosis resemble those reported from Western countries. With early onset, UC may be difficult to distinguish from CD using laboratory values. ESR is a useful marker for disease activity at time of diagnosis in both UC and CD.

P024. Vitamin d levels in children living in england

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Introduction; Paediatric IBD patients living in England are prone to develop low Vitamin D (VitD) levels due to limited sun exposure, low oral intake, malabsorption and indoor resting. VitD monitoring has become a standard of quality in IBD care over the past years as low levels have shown to be detrimental in children for their bone health and possible for the disease itself. Aims: To assess guidelines compliance for yearly VitD monitoring and to determinate the frequency of deficiency and insufficiency.
Methods: We retrospectively reviewed all VITD levels performed locally and from district hospitals for IBD children diagnosed over the past 5 years. VITD insufficiency was defined between 25-75nmol/L and deficiency when <25nmol/L. We compared the proportion of patients who were yearly assessed, patients with normal and insufficient levels, and IBD subtype. Descriptive analysis was performed.

Results: 51% (n=96) of patients had VITD determination at least once over the past 3 years. When grouped by year, 21 patients had vitamin levels in 2014, 43 in 2015 and 66 in 2016. This represents a 3 fold increase within an average IBD population of 188 patients. 15.6 % (15/96) were VITD deficient (6 CD, 5 IBDU, 4 UC) at least in one determination, 60.4% (58/96) were VITD insufficient (26 IBDU, 24 CD, 8 UC) at least in one determination over the past 3 years. All patients who were VITD deficient had normal levels after 2-3 months of VITD treatment.

Conclusion: A considerable improvement in the standard of care has been achieved by increasing the yearly rates of VITD determination among our patients. VITD deficiency and insufficiency were common as described in other geographic regions. VITD monitoring enable us to identify patients at risk of abnormal bone health and to promptly commence vitamin D supplementation when low levels are found.

P025. Pediatric IBD patients do not meet the minimum daily requirements of vitamin d and calcium intake: tertiary centre survey-based analysis

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Introduction: Achieving optimal levels of vitamin D (VITD) and calcium (Ca) is essential for developing children. Sufficient oral intake in IBD children is difficult for multifactorial reasons.

Aim: To assess if paediatric IBD patients follow the recommendations made by the British Scientific Advisory Committee on Nutrition and the United Kingdom Department of Health concerning VITD and Ca oral intake

Methods: A prospective dietetic survey was conducted among sequential 151 IBD children over a 12 month period. VITD and Ca intake were assessed through a 24 hour recall of dietary intake questionnaire. Children on restricted diets for allergic disease and less than 4-year-olds were excluded. Patients were grouped into 4-10 and 11-18 years. Sources of VITD and Ca were divided into dairy, oily fish, fortified cereals and egg. Descriptive analysis was performed.

Results: Survey conducted represents 68.3% of all IBD patients under follow-up. 94 patients were included for analysis. Overall, only 26.6% and 21.3% of the surveyed population achieved the current recommended intake for Ca and VITD respectively. In the younger group, only 7/31 (22.6%) met the current VITD recommendations, the same figure repeats with regards Ca intake. In adolescents, only 13/63 (20.6%) and 18/63 (28.6%) met Ca and VITD recommendations respectively. In both groups dairy was the main source of VITD (61.3% and 58.7%). Less than 1/3 of the patients have an optimal intake of oily fish and egg (sufficient intake 19%, 9% for children and 30%, 26% for adolescents).

Conclusions: Paediatric IBD patients living in the UK do not meet the minimum requirements of VITD and Ca intake and therefore are at risk of having poor bone health, calcium homeostasis imbalance and VITD deficiency. In the great majority, Ca and VITD sources come from dairy whereas the contribution of oily fish and egg as a VITD source is minimal.

P026. Risk factors for vitamin D deficiency in children with Crohn’s disease or ulcerative colitis: a retrospective cohort study in Canada.

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BACKGROUND: While the effects of low vitamin D (VITD) levels on the severity of inflammatory bowel diseases (IBD) have been recently described in adults, little is known about the risk factors associated with such deficiency in children. In addition, there is a lack of guidelines regarding the frequency of VITD monitoring.

OBJECTIVES: The aim this study was to investigate the clinical and biological factors that could predict the risk of low VITD levels.

METHODS: In our IBD database, we identified patients with Crohn’s disease (CD) or ulcerative colitis (UC) who had at least one VITD blood level drawn, either at diagnosis or during follow-up, between 2010 and 2016. VITD analysis was performed using tandem mass spectrometry. The patients were classified in two groups (low or normal VITD; cut-off: 75 nmol/L). Potential factors associated with low VITD were analyzed with chi-square test or T-Tests. A multivariate logistic regression was then performed.

RESULTS: 285 patients (mean age 12.4±3.72; 193 CD; 125 males) had a total of 681 VITD tests (mean 2.5 tests/patient). At diagnosis, 80.7% patients had low VITD (median[IQR]: 55(26) nmol/L). Among patients with the first sample taken during follow-up, only 31.5% of CD and 40.6% of UC had normal VITD. In multivariate analysis, blood samples taken during autumn or winter were associated with a greater risk of low VITD as compared to summer (respective odds ratios(OR): 3.43(1.39-8.47) and 8.32(2.98-23.2)). The risk was also higher in presence of anemia (OR: 1.64(1.03-2.62)) and high CRP levels (OR: 1.01(0.99-1.03)). Including all these factors in the same model, the area under the ROC curve was 0.7644.
CONCLUSION: Winter and autumn seasons and anemia are strongly associated with a risk of low VITD. We recommend that blood samples for VITD should be drawn for every child at diagnosis and controlled at least yearly, especially during autumn and winter.

P027. Abnormal bone mineral density in patients with Pediatric inflammatory bowel (PIBD) disease in a tertiary hospital

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Introduction: Significant deficit in bone mass has been observed in PIBD. This deficit may affect the attainment of peak bone mass, which is the most important determinant of long term skeletal health, as well as linear growth. Dual energy X-ray absorptiometry (DEXA) is the preferred technique for assessing children’s bone health.

Aims: To assess bone mineral density status in PIBD patients seen in a tertiary centre.

Methods: Retrospective review of the first DEXA scan performed to PIBD patients between 2010-2016. Risk factors and reason for request were collected. L2-L4 spinal bone density was considered for analysis (GE Lunar Prodigy Advance Bone Densitometer), the score was adjusted according to age, ethnicity and body size to obtain a volumetric bone mineral apparent density (BMAD) score as recommended by the UK National Osteoporosis Society. DEXAs were classified as normal, suboptimal and low (BMAD-score < -2.5, ≤ -2.1 ≤ and <1 respectively). Descriptive analysis was performed.

Results: 44 DEXA scans were performed over a 5-year period (2.9 scans/343 patients/year), 29 were first-time requests. Majority were males (n=19, 66%), 17 (59%) corresponded to CD patients, 4 were UC (18%) and 8 IBDU (28%). Reason for requesting the test obeyed at least to one risk factor in 23 cases (fractures n=4, persistent inflammation n=5, long term steroids n=13, poor growth/ lean mass deficit n=12), in 2 cases due to bone pain and in 4 cases as screening shortly after diagnosis. 20/29 (68.9%) scans were abnormal (11 suboptimal and 9 low). Mean BMAD score was -1.25, median -1.56 and SD 1.42. Details depicted in graph 1.

Conclusions: Low and suboptimal bone density was common in this group of patients. The majority had at least one risk factor for impaired bone health. Clinicians are advised to routinely screen bone density status in patients at diagnosis and when risk factors are present.

P028. Bone health assessment in pediatric inflammatory bowel disease at diagnosis

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Background and objectives: Pediatric Inflammatory Bowel Disease (PIBD) is a chronic disease that can produce a negative impact on growth and bone mineral density (BMD), increasing the risk of fractures. The mechanism is not clearly elucidated but both the inflammation and some other factors are involved. Our aim is to evaluate bone health in PIBD patients at diagnosis.

Methods: Descriptive, retrospective study of PIBD patients diagnosed between 2014 and 2016 in our center. Baseline clinical, epidemiological and analytical data were recorded. Dual energy X-ray absorptiometry (DXA) and Vitamin D values were performed at diagnosis. The analysis was realized with program SPSS v.21.

Results: Seventy-three patients (74% male; 52 Crohn’s, 21 Ulcerative Colitis) were included. Mean age at diagnosis: 12.9 years; mean diagnostic delay 3 months. Mean baseline vitamin D value was 25.4 ng/ml; 32.2% had vitamin D deficiency (<20 ng/ml) and 41.9% suboptimal levels (20-30 ng/ml). Regarding DXA, the Z-Score mean value in total body was -0.33 SD and in lumbar spine -0.41SD. 22.1% of the patients had low BMD (Z-score between -1 and -2 SD). No correlation was found between vitamin D levels and DXA (80% of patients with abnormal DXA had normal vitamin D). Other analytical, clinical and nutritional markers (CRP, ESR, PCDAI or PUCAI, small bowel involvement in CD, diagnosis delay or Waterloo Index for weight) showed non statistically significant differences between patients with normal or abnormal BMD (P>0.05).

Conclusions: The evaluation of vitamin D deficiency and bone mineral density in PIBD patients is of great importance in order to establish an early treatment and an appropriate follow-up. The assessment of dietary habits is mandatory in order to avoid deficiencies that may negatively influence bone health. In our series more than 30% of patients requires specific therapy intervention to improve bone health.

P029. Bone mineral density as marker of nutritional status in pediatric IBD

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BACKGROUND AND OBJECTIVES: Inflammatory bowel disease (IBD) is known to be a risk factor for osteopenia and osteoporosis. It has a multifactorial pathogenesis and its supposed to be from the beginning of the illness. The aim of the study is to know the status of the bone mineral density (BMD) at diagnosis of IBD in our pediatric population.

METHODS: Retrospective review of all pediatric patients referred to our unit for diagnosis of IBD since the last 5 years. The BMD is performed with DXA on lumbar spine in all patients and is expressed by z-score.

RESULTS: 33 patients were included. 63% Claire, 60% Ulcerative Colitis (UC). 40% Crohn’s Disease (CD). Mean (±SD) age at diagnosis of IBD was 11.24 (±2.17) years. The median BMD z-score was -0.1 (interquartile range: -1.1 to +0.25), which is normal rate in general population. Osteopenia defined as z-score ≤ -1SD was found in 30.3% of the patients (n=10), and osteoporosis defined as z-score ≤ -2SD was found only in 1 patient (3%) with a severe CD at diagnosis. There was no significant difference between UC and CD in: age at diagnosis (p=0.98), weight and height at diagnosis (p=0.168, p=0.57), fecal calprotectin (p=0.42), and BMD (p=0.12). Based on activity scores at diagnosis UC patients have more severe illness (PUCAI 35-60 in 75%) than CD ones (PCDAI 10-27 in 50%). Among the
osteoopenic patients there was no statistically difference regarding: gender, UC or CD, fecal calprotectin and height, but this group showed less weight and body mass index (p<0.05) at diagnosis of IBD vs the patients with no osteopenia.

CONCLUSIONS:
- Osteopenia but not osteoporosis is present at diagnosis in IBD pediatric patients.
- There is no difference in BMD between CD and UC patients at diagnosis.
- The z-score BMD approximates to normal population rates at diagnosis.
- Less weight and body mass index are associated to the presence of low BMD.

KEYWORDS: osteopenia, osteoporosis, nutritional status

P030. Body composition analysis using bioelectrical impedance in Pediatric patients with Inflammatory Bowel Disease

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Introduction: Paediatric Crohn’s Disease (CD) is associated with malnutrition, weight loss, osteopenia and failure to thrive. These deficits could result an altered body composition.

Aim: Our aim was to compare the body composition in children suffering in CD and an age matched control group, and to follow the changes in the body composition in CD patients getting exclusive enteral nutrition (EEN) and using biologics (anti-TNFα).

Materials and methods: Body composition was measured in CD patients (n=15, mean age: 15.4 years) using bioelectrical impedance at the beginning of the therapy they received, and 6-8 weeks later. Six patients were treated with EEN, eight patients received anti-TNFα therapy. Healthy (n=9, mean age: 15.21) and CD patients (n=7, mean age: 13.11) in remission as controls were enrolled in the study. In parallel, we followed the alterations in the body composition in the treated children during their therapy. We calculated the z-scores using Joubert-method.

Results: Patients in active phase had lower values compared to the patients in remission phase and healthy controls (HC): weight z-score (-0.8 vs. 0.4 and 0.3), fat mass index (FMI: 3 vs. 5.2 and 4.6) and fat free mass index (FFMI: 14.2 vs. 16.3 and 14.5). During the EEN therapy the weight z-score (from -0.9 to -0.7), the FMI with 0.07%, and the FFMI with 2.76% increased. In patients who react to biologics the z-score increased with 0.12, the FMI 3.66% and the FFMI with 2.33%. The values in therapy resistance group decreased: weight z-score: with 0.5, FMI with 11.5%, and FFMI with 9.9%.

Conclusion: During the EEN the parameters did not change significantly. Through the induction of anti-TNFα therapy clear difference between patients who responded and non-responded were detected. In conclusion, the induction of biologics and the EEN may have an effect on body composition.

P031. Pediatric inflammatory bowel disease and attained final height-a population based cohort study

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Background and objectives We aimed to examine the influence of pediatric inflammatory bowel disease (IBD) on attained final height and on the risk of growth retardation.

Methods Nationwide cohort study. We identified 3526 individuals diagnosed with pediatric IBD between 1990-2014 (Crohn’s disease (CD): n=1417; ulcerative colitis (UC): n=1803; IBD-Unclassified (IBD-U): n=306) using data from the Swedish Patient Registry. Index individuals were matched with up to ten reference individuals for age, sex, birth year and place of residence (n=29,409). Biological parents and full siblings (n=3788) were identified through the Multigeneration register. Data on final height (defined as height measurements after the 18th (women) or 20th (men) birthday) were obtained through National Registers.

We used fixed effects linear regression to analyze the effect of IBD on the average height adjusted for target height, the matching variables and socioeconomic markers. We used logistic regression for the binary outcome of growth retardation. These outcomes were also examined in sibling analyses.

Results Children with IBD had shorter final height (adjusted mean difference (95%CI): -0.9cm (-1.1 to -0.7). Girls and boys were equally affected. The height difference between IBD-patients and matched comparators was more pronounced in CD than in UC (-1.3cm vs -0.7cm), and most prominent in patients with onset before puberty (-1.4cm (-1.8 to -1.0)) or requiring bowel surgery (-1.9cm (-2.4 to -1.4)).

IBD patients had an increased risk of growth retardation defined as >8.5cm shorter than target height OR (95%CI): 2.1 (1.7-2.5). Patients undergoing bowel surgery during childhood had a 3.5-fold increased risk of growth retardation. When restricting the analyses to siblings, the association between final height and IBD remained.

Conclusion Childhood with IBD have a slightly shorter adult height and an increased risk of growth retardation. The effect of IBD on final height is modest.

Keywords: pediatric IBD, attained final height
P032. Phenotype, treatment and outcome of patients with very early onset IBD and infantile IBD: results from the cedata-gpgpe registry

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Background & Objectives: Patients with very early onset inflammatory bowel disease (VEO-IBD, < 6 yrs at diagnosis) and infantile IBD (< 2 yrs at diagnosis) are often selectively reported from tertiary centres. We used data from a large prospective registry of the society for Paediatric Gastroenterology and Nutrition from Germany and Austria (CEDATA-GPGPE).

Methods: Data on paediatric IBD patients were prospectively obtained by questionnaires at diagnosis and during follow up from 96 reporting clinical institutions. Phenotype, treatment and outcome of VEO-IBD patients (group1) were compared with patient groups 2 (aged ≥6≤10 years) and 3 (aged >10 years). Follow-up data were obtained by an extended questionnaire for patients with infantile IBD.

Results: The characteristics of 4160 included patients are shown in table. VEO-IBD patients (n=423) were more often diagnosed with ulcerative colitis (UC) or IBD-U (45.4% and 14.2%, respectively) than children in group 2 (36.3% and 7.6%) and group 3 (30.6% and 5.2%). VEO-IBD children changed more commonly the diagnosis (mostly from UC or IBD-U to Crohn’s disease) and suffered less often than older children from fistula, abscesses and stenosis. Children in group 2 had a higher risk for surgery than younger and older age groups (8% versus 4.3%; 5.1%). The survey on 40/64 infantile IBD (median follow-up 8.2 years) yielded four with a primary immunodeficiency disease (2 x IL-10-R deficiency, XIAP deficiency, IgA deficiency), of which one died from septic shock. Two children developed lymphoma, three were diagnosed with autoimmune diseases. At the time of last follow up, 33/40 were in remission, 10/33 without medication.

Conclusion: VEO-IBD patients in this unselected patient cohort differ in many aspects from patients diagnosed during school age. In infantile IBD immunological work-up was incomplete, and may explain the low proportion with immunodeficiency disorder (10%). Prognosis was excellent in 25% of infantile IBD patients.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
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<tr>
<td></td>
<td>(infants ≤2y)</td>
<td>(2-6y)</td>
<td>(6-10y)</td>
<td>(&gt;10y)</td>
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<tr>
<td>Median age at diagnosis, (yrs)</td>
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<td>4.2</td>
<td>4.0</td>
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<tr>
<td></td>
<td>(0-1.9)</td>
<td>(2-5.9)</td>
<td>(0-5.9)</td>
<td>(0-19.5)</td>
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<tr>
<td></td>
<td>(59-73)</td>
<td>(46-71)</td>
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P033. Evaluation of Autonomic Nervous System Functions in Children with Inflammatory Bowel Disease in Remission

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Objectives and study: Ulcerative colitis (UC) and Crohn disease (CD) are inflammatory bowel diseases (IBD) with unknown etiology. Recent studies show, chronic inflammation, stress, medications and malnutrition lead to develop autonomic nervous system (ANS) dysfunction in IBD. In this study, we evaluated the effect of IBD on ANS functions by using noninvasive electrophysiological parameters like heart rate variability (HRV) in young patients.

Methods: Thity-five IBD patients in remission phase, between the ages of 3 and 18, were enrolled in the study, who have been followed-up in our pediatric gastroenterology department for at least 12 months. Thirty-five age and sex matched healthy individuals were chosen as the control group. Clinical and laboratory parameters of all the individuals were evaluated. Previous structural heart disease was excluded with physical examination and echocardiographic assessment.

Results:

- The study group had 15 UC and 20 CD patients; and sex and age matched 35 healthy children. The mean age was 11.96 ± 4.47 in patients and 12.01 ± 4.2 in controls, with 51.4% (N=18) female and 48.6% (N=17) male individuals. Minimal and mean heart rate was significantly higher and the mean RR interval was significantly lower in patients comparing to controls. Besides, out of time dependent HRV parameters, SDNN day, SDNNi and SDANN indexes were significantly lower in patients (p<0.05), in addition, out of frequency dependent HRV parameters, VLF and LF were also significantly lower (p<0.05) in this group.

Conclusion: Since this autonomic dysfunction we found in young IBD group may be related with increased cardiac morbidity and mortality in older age, we believe that long term cardiac follow-up might be necessary in this group of patient.
P034. An examination of the clinical outcomes of ulcerative colitis patients with mucosal atrophy in the Irish centre for Pediatric gastroenterology

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Introduction: Mucosal atrophy of the colon describes irregularities in the morphology and distribution of the intestinal glands of the mucosa.

Aims: The principal aim of this study was to investigate the prevalence of mucosal atrophy in new-onset paediatric UC patients between 1st January 2012 and 31st July 2016. Secondary objectives were to compare how patient demographics, disease activity, medical therapy and growth outcomes differed from those without mucosal atrophy. The final aim was to evaluate the incidence of paediatric UC in the Irish population.

Materials and Methods: Patients were diagnosed according to the Porto criteria. Mucosal atrophy was identified from histopathological reports. Patients were phenotyped using the Paris classification. Disease activity was analysed using the Paediatric Ulcerative Colitis Activity Index. Standardised incidence per 100,000 per year was calculated using Poisson regression analysis using population data from the Central Statistics Office (CSO) “Statbank” database. Statistical analysis was conducted using SPSS Version 24.0

Results: 163 patients diagnosed with ulcerative colitis were included, of which 77 male. The total mean incidence of paediatric ulcerative per year was 3.15 per 100,000, this rate is stable. Incidence in the age group 0-4.9 is increasing. Seventeen cases of mucosal atrophy were identified in the total cohort, 9 male. Compared to patients without mucosal atrophy, those with mucosal atrophy had higher disease activity scores at three month (p=0.04), six month (p=0.01) and two year follow up (p=0.01). They also showed higher rates of progression to immunomodulators and biologics. Finally, these patients were more likely to ever relapse (p=0.04) and had significantly shorter time to first relapse event post diagnosis (p=0.01).

Conclusion: Paediatric ulcerative colitis patients with mucosal atrophy demonstrate higher disease activity scores and rates of relapse, and higher rates of progression to immunomodulators and biologics

P035. An examination of the effect of deep ulceration on clinical outcomes for patients with Crohn’s disease.

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Background and Objectives: The aims of this study were to examine the incidence of deep ulceration in a paediatric population and to better understand the impact of this disease behaviour on clinical outcomes.

Methods: Determinants and Outcomes in Children and Adolescents with IBD (DOCHAS) is a prospective study following Irish children newly diagnosed with IBD. Patients were recruited between 1st January 2012-31st July 2016. Patients, diagnosed according to the Porto criteria were rigorously phenotyped using the Paris Classification. Information was uploaded to an online database and analysed using SPSS.

Results: One hundred and sixty one patients were diagnosed with Crohn’s disease. Incidence rates increased from 1.98 to 3.89 per 100 000 per year between 2012 and 2016. One hundred and nineteen (74%) patients in this study were male, of which 43% (n = 70) had deep ulceration at diagnosis. Baseline PCDAI was higher for patients with deep ulceration compared to those without deep ulceration (39.1 and 31.7 respectively, p = 0.003). Patients with deep ulceration relapsed earlier than...
those without deep ulceration (3 ± 0.9 months versus 7 ± 0.9 month, p = 0.027). They also had a higher mean calprotectin level at 12 months compared to those without deep ulceration (1451 ± 1080 versus 154 ± 130, p =0.02). The odds of being in remission were higher in patients treated with exclusive enteral nutrition (OR = 2.259) in comparison to immunomodulators and biologics at one year (OR = 1.121, and 0.833 respectively).

Conclusion: Children with deep ulceration have a more severe clinical presentation at diagnosis. Despite being in clinical remission children with deep ulceration had active mucosal disease one year post diagnosis based on calprotectin levels. This suggests that children with deep ulceration require more aggressive therapeutic intervention to induce endoscopic remission.

Key Words: Crohn’s disease, Deep ulceration, Incidence

P036. Association between clinical and pathological findings in pediatric onset IBD patients, a retrospective analysis from a tertiary center

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Background and Aim: We aimed to investigate the difference between 3 age groups of IBD (younger than 2 years of age, 2-10 years and 10-17 years of age) as a retrospective analysis. We included symptoms, lab results, colonoscopic and histopathological findings which are followed in a tertiary center. We performed a retrospective analysis of data collected from 71 children (0-17 years old) with pediatric IBD between 2003 and 2016. We classified patients according to the Pediatric Paris modification of the Montreal classifications and compared age of the symptom’s onset and diagnosis, the first presentation of patients, clinical, laboratory and imaging findings of them. 6 patients had infantile onset IBD (younger than 2 years of age), 19 had Early onset IBD, EoIBD, (younger than 10 years of age) and 45 had Pediatric onset IBD (younger than 17 years of age). Among this children, time between the first symptoms and the diagnosis ranged between 1 and 76 months with mean being 12.69 ± 16.02 months. In 81% of the children fecal calprotectin was measured and 10% of these was less than 50 μg/g, 15% was between 50-200μg/g, and 75% was greater than 200 μg/g.

In order to determine the histopathological results of GI involvement, mucosal biopsy was obtained which showed cryptitis (39%), crypt abscess (25%), plasma cell infiltration (23%) and basal plasmacytosis (23%). The most frequent presentation of the patients was diarrhea(77%), followed by abdominal pain (75%), and bloody diarrhea (63%). Laboratory results showed elevated CRP (87%)and sedimentation rate(65%). Total blood count of the patients revealed anemia(55%) and thrombocytosis(46%).

Before the treatment 63% of the children had histopathologically active disease whereas this number diminished to 22% after the appropriate treatment.

P037. Diagnostic Gastroscopy Predicts Outcome Following Right Hemicolectomy in Pediatric Crohn’s Disease

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Introduction: Paediatric Crohn’s disease has been shown to have a high recurrence post-surgical resection. Previous surgical resection, penetrating disease and smoking have been identified as risk factors for early postoperative recurrence.

Aims: The aim of this study was to identify factors that influence CD recurrence following right hemicolectomy in paediatric patients.

Materials and methods:Paediatric CD patients who underwent a right hemicolectomy were identified on databases at the Royal London hospital and Massachusetts General Hospital from year 2000-2013 and 2000-2014 respectively. In this retrospective observational study, CD patients were subdivided into the relapse group with
clinical, endoscopic, radiological and/or histological CD recurrence, and the non-relapse group. Data analysed included patient demographics, diagnostic gastroscopy and colonoscopy findings, Montreal classification, operation details, pre-operative and post-operative pharmacotherapy, relapse and additional follow-up information. Results: 96 patients were identified, of which 57 relapsed post-operatively with a median time of 1.88 years to relapse. A higher proportion of children who relapsed were males (p=0.004). CD with ileocolonic involvement was associated with CD recurrence (p=0.022). Children with abnormal diagnostic gastroscopy histology findings had a higher rate of CD recurrence, with a cumulative recurrence of 82.2% at 10 years, compared to those with normal diagnostic gastroscopy findings, with a recurrence of 42.7% at 10 years (Hazard ratio 3.42, p=0.001, 95% CI 1.86 to 6.30). Multivariate analysis showed that abnormal diagnostic gastroscopy was a significant predictor for CD recurrence (Odds ratio 1.37, p= 0.011). Patients who altered their pharmacotherapy post-operatively had a lower incidence of CD recurrence (p=0.0065).

Conclusion: This multicentre retrospective study showed a number of risk factors for post-operative CD recurrence. Most interestingly, patients with abnormal diagnostic gastroscopy had an increased risk of recurrence. This is the first study to demonstrate that abnormal diagnostic gastroscopy findings is a predictive factor for post-operative paediatric CD recurrence.

P038. Differences between pediatric and adult IBD – analysis based on the data from multicenter, prospective cohort observational SATIMOS study.

Joanna Sieczkowska-Golub1, Dorota Jarzebicka1, Agnieszka Borys – Iwanicka2, Anna Korłatowicz- Bilar1, Anna Szafiarska-Popławska2, Urszula Grzybowska-Chlebowczyk3, Izabela Lazowska-Przeorek4, Urszula Daniluk5, Bartosz Korczowski6, Beata Sordy6, Mariusz Szczepaniak7, Piotr Landowski8, Anna Płociek9, Katarzyna Bąk – Drabik10, Edyta Zagoświcz11, Jarosław Kierkus1

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Backgrounds: Biological treatment is actually easy available for inflammatory bowel disease treatment.

Aim: The aim of assessment was to compare disease presentation between children and with Crohn’s disease(CD) and ulcerative colitis(UC) qualified to anti-TNF therapy.

Methods: A multicenter, prospective cohort observational study to assess efficacy and prevalence of AE in Polish cohort was started at 01.2014. To study were included all patients in every age who started anti-TNF therapy.

Results: Time from first symptoms to diagnosis varied between type of disease and age. Mean time for diagnosis was 4 months for UC and 6.9 months for CD in ical Hospital No. 1 of Silesian Medical Institute, Lodz, Warsaw, Warsaw, 7Department of Pediatrics, Gastroenterology and Allergology University Hospital in Białystok, Białystok, 8Department of Pediatric Gastroenterology Regional Clinical Hospital No. 2 in Rzeszów, Rzeszów, Poland, 9Department of Gastroenterology, Allergy and Pediatrics Polish Mother’s Memorial Hospital Research Institute, Lodz, Warsaw, 10Department of Gastroenterology and Metabolic Diseases Clinical Hospital of Medical University in Poznań, Poznan, 11University Clinical Center , University Hospital Department of Gastroenterology, Gdańsk, 12Department of Allergology, Gastroenterology and Nutrition, Children Central Hospital of Medical University in Łódź, Lodz, 13Department of Pediatric Independent Public Clinical Hospital No. 1 of Silesian Medical University in Katowice, Zabrze 14Department of Gastroenterology Oncology Oncology Centre - Institute for them. Mania Skłodowska – Curie in Warsaw, Warsaw, Poland

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Methods: A multicenter, prospective cohort observational study to assess efficacy and prevalence of AE in Polish cohort was started at 01.2014. To study were included all patients in every age who started anti-TNF therapy.

Results: Time from first symptoms to diagnosis varied between type of disease and age. Mean time for diagnosis was 4 months for UC and 6.9 months for CD in pediatric population vs 7.8 months and 12 months in adults, respectively. At the moment of anti-TNF qualification 58,0% adults and 60.4% children had E3 severity in Montreal classification. Among CD patients the most common disease localisation in children were colon (40.2%) and terminal ileum (44.3%), terminal ileum in adults were affected only in 29.3%. The most common disease localisation in adults were large intestine (44.3%). Upper digestive tract were 4 times more common affected in children 27.1%; vs 7.2% in adults. Mean time from diagnosis to treatment with biologic therapy was 1.4 y among UC patients were 2.0 y for children and 4.3 y for adults.

Conclusion: Pediatric patients mostly have more aggressive form of disease what lead to earlier disease diagnosis and earlier need of anti-TNF treatment. In comparison to adults, in children with CD localisation is more common in terminal ileum and upper digestive tract.

P039. Inflammatory Bowel Disease in Children with Special Health Care Needs

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National Center For Child Health And Development, Tokyo, Japan

Introduction There have been a few report of inflammatory bowel disease (IBD) in children with special health care needs (CSCHCN). We have encountered a number of CSHCN who developed IBD. The characteristics of IBD in CSHCN has not been well documented.

Methods A database of patients with IBD seen at National Center for Child Health and Development in Japan between August 2006 and April 2017 were retrospectively reviewed. For CSHCN with IBD, their underlying diseases, clinical characteristics, and clinical courses were analyzed.

Results Among 178 cases of IBD (100 UC, 76 CD, 2 IBD-u), five of 100 UC (5/100, 5%) were CSHCN (M:F=3:2, median age of onset:36 months (24-49), median age of diagnosis: 38 months (28-50)). The median follow up period after the diagnosis was 35 months (23-263). All had epilepsy and dysphagia, and required anticonvulsives and tube feeding at diagnosis. Three had asthma and four had tracheostomy placed. None of them were complicated with primary sclerosing cholangitis. The presenting symptom was bloody diarrhea in all cases. The disease extent at diagnosis was E4 (pancolitis) by Paris classification in all five. Although there was a girl who required only 5-ASA to induce and maintain remission of UC, other four became steroid-dependent or -resistant and required second line treatment. Azathioprine was used in all 4, tacrolimus in 3, and biologics in 2. One child had subtotal colectomy with ileostomy 10 years after the diagnosis for her steroid resistant course. One steroid dependent child developed idiopathic ARDS, and died at 23 months after the diagnosis.
Conclusions Our 5 CSHCN with IBD were very early onset-UC, and CSHCN may have higher incidence of UC compared to healthy other population. Their disease were extensive, and appeared to be refractory to conventional treatment.

Keywords Ulcerative colitis, Children with special health care needs, very early onset

**P040. Disease phenotype of korean pediatric Crohn’s disease patients at diagnosis: a multicenter retrospective comparative study with eurokids**

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**Introduction**

There is limited data regarding the disease phenotype of pediatric Crohn’s disease (CD) patients in the Asian population.

**Aims**

To investigate the disease phenotype of Korean pediatric CD patients at diagnosis according to the Paris classification by comparison with the published EUROKIDS data.

Materials and Methods

Korean children and adolescents who were newly diagnosed with CD before 18 years-old during January 2013 to October 2016 were included in this multicenter retrospective study. Medical charts were reviewed and disease phenotype at diagnosis was classified according to the Paris classification. Comparison was performed by utilizing data from the previously published 5-year analysis of the EUROKIDS registry.

Results

A total 230 subjects (150 males, 80 females) were included. The median age at diagnosis was 14.7 years (range: 1.2-17.9). No significant difference was observed in M:F ratio compared with EUROKIDS (1.88:1 vs. 1.46:1, p=0.088). A complete workup was done in 213 subjects. The proportion of children <10 years (A1a) was significantly lower in Koreans (6.6% vs. 19.6%, p<0.001). Colonic disease was less prominent (9.9% vs. 27.3%, p<0.001), while upper GI involvement was more prominent in Korean children (60.1% vs. 46.2%, p<0.001). Although no significant difference was observed in luminal disease behavior, the proportion with perianal modifiers were significantly higher in Korean patients (46.5% vs. 8.2%, p<0.001). Meanwhile, a first-degree family history of inflammatory bowel disease was significantly lower in Korean children (4.8% vs. 10.8%, p=0.005)

Conclusions

Newly diagnosed pediatric CD patients in Korea are more likely to present at an older age, with more ileocolonic and upper GI tract involvement, and perianal fistulas and/or abscesses, compared to their counterparts in Europe. An underlying genetic difference between races may play a role in the different expression of phenotypes in pediatric CD.

**P041. Malignancy and mortality in pediatric-onset inflammatory bowel disease: a systematic review**

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**Introduction**

Better insight in the characteristics of pediatric-onset inflammatory bowel disease (PIBD) patients that develop cancer or fatal outcome will help to identify predictive factors of severe disease course, which are ultimately needed to further optimize therapeutic strategies.

**Aims**

We conducted a systematic review to provide an overview of all reported PIBD patients with a severe outcome.

**Material and methods**

A literature search identified publications that reported development of cancer or fatal outcome in PIBD patients. Studies were eligible for inclusion when (1) article written in English, (2) original data, (3) individual patient information and (4) full text available, (5) study population consisting of patients diagnosed with IBD <19 years, who (6) developed cancer or had a fatal outcome at any point later in life.

**Results**

The search yielded 9,629 articles, of which 6,608 articles were excluded based on title or abstract. A total of 94 studies were included which comprised data of 261 PIBD patients who developed cancer and/or fatal outcome at any point later in life. Most identified studies were case reports (n=48), case series (n=11) and retrospective cohort studies (n=28). Five prospective cohort studies, 1 cross-sectional study and 1 case control study were retrieved. The most frequent type of non-fatal cancer was lymphoma, whereas colorectal carcinoma was the most frequently reported type of fatal cancer. The majority of patients with non-cancer related fatal outcome were diagnosed with ulcerative colitis and most often died due to infectious complications.

**Conclusions**

The data in this review suggest that PIBD associated malignancy and mortality is rare, detailed clinical characteristics are limited, and that long-term follow-up of PIBD is crucial to identify severe outcomes. Prospective and international collaborations are needed to obtain better insight in the characteristics of PIBD patients that develop cancer or fatal outcome.

Keywords: PIBD, malignancy, mortality

**P042. Global variation in use of exclusive enteral nutrition for pediatric Crohn disease**

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**Background and Objectives**

Exclusive enteral nutrition (EEN) is an excellent induction treatment for pediatric Crohn disease. Although guidelines are available, there is significant centre-based variation in the use of EEN. Given the paucity of validated tools to identify practice variation we constructed a survey aimed at sharing experience and strategies in administering EEN, stimulating further research, and optimizing EEN therapy.

Vol. 65, Supplement 1, October 2017
Methods: As there is no validated questionnaire available, this survey was constructed after consultation with experts in the field and designed to address key gaps in knowledge. The survey was disseminated through personal invitation (to the Porto group; Canadian Children IBD Network; selective experts in the field) and sent twice through the PEDGI-BB. Responders were encouraged to involve others in their group, especially dietitians and nurses. The survey remained open for a period of 3 months (summer of 2016). Data were collected into RedCap and analyzed using descriptive statistics.

Results: In total, 146 participants from 26 countries completed the survey. Eighty-Nine participants were from Europe (including UK and Israel), 41 from North America, and 16 from elsewhere. Sixty-five percent of participants were general, non-IBD-focused pediatric gastroenterologists, 21% were IBD-focused, 10% dietitians. The most common indications (~90% use) were for ileocecal and ileocolonic disease (Paris L1 and L3); 52% indicated use for isolated colonic disease (L2). The most common duration was 8 weeks and 66% preferred oral administration. Most (63%) did not allow any additional intake and 69% instructed patients to continue partial EN after completing treatment. Dietitians were identified as essential to EEN success, while the primary challenges were adherence and lack of support.

Conclusions: We found significant variation in practice and use of EEN, with several regional effects. Global differences in practice offer opportunities for research and improving care. This survey establishes a framework for collaboration and information sharing.

P043. Does standard therapy in Pediatric Crohn’s disease really prevent our patients from the need of early initiation of anti-TNF treatment?

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Background: ECCO-ESPGHAN guidelines recommend the use of EEN (6–8 weeks) combined with early use of immunomodulators (IMM) as the optimal therapy in these patients at diagnosis. However, a high rate of relapse after EEN has been reported. Moreover, the potential effect of this strategy in postponing or avoiding the future need of biological treatment has not been evaluated. Our aim is to determine the proportion of CD patients diagnosed in the last years in our Centres and treated with EEN and thiopurines at diagnosis have required escalation to anti-TNF treatment during their follow-up.

Methods: Data from CD pediatric patients diagnosed between 2007 and 2014 who entered remission with EEN combined with thiopurines were retrospectively collected. The percentage of patients that needed to escalate to anti-TNF therapy (infliximab or adalimumab) after failure of maintenance treatment during their follow-up in our Unit was analysed. Results: In total, 110 patients, 70 boys with a mean age at diagnosis 12.2±2.9 years fulfilled the inclusion criteria. In 60 patients (54.9%), anti-TNF treatment was started, 24 received IFX and 36 ADA. The age of initiation of treatment was 13.2±2.3 years and the time from diagnosis of 10 months (IQR 4.5-20.5). We did not find any differences between both anti-TNF regimens in terms of age [IFX 13.7(IQR 11.0-14.8) vs ADA 13.5(IQR 11.7-14.9), p=0.718] or time from diagnosis [IFX 11.8(IQR 4.0-20.0) vs ADA 9.85(IQR 4.6-24.5), p=0.375]. Mean follow-up was 3.6 years (IQR 1.6-5.8).

Conclusion: The use of EEN has proved to be effective for the remission of paediatric CD and may delay somewhat the use of biological treatment. Further studies showing the long-term follow-up of patients treated with standard therapy (EEN and immune-modulators) are needed to know the real effect of this combination in avoiding initiation of biological therapy.

P044. The gut virome of pediatric Crohn’s disease (cd) following exclusive enteral nutrition

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Background and Objectives: Sustained remission accomplished by exclusive enteral nutrition (EEN) is associated with changes in the gastrointestinal microbiome. Although most research in IBD pathology to date has been focused on genetic variants and gut bacteria, little has been uncovered about the contribution of the gut virome. The gut virome has been shown to be abnormal in adult IBD patients, and we recently showed that the mucosal virome at baseline is important for predicting sustained remission in pediatric CD patients.

Our aim was to optimize characterization of the gut virome in response to EEN treatment and to identify longitudinal viral-bacterial interactions.

Methods: Metagenomic shotgun sequencing (MGS) was carried out on 10 stool samples enriched for free viromes from 7 pediatric patients with CD and 1 with undefined IBD. Viral taxonomy of each sample was determined by aligning MGS reads against the viral component of the NCBI RefSeq database. Bacterial taxonomic profiles were generated using 16S rRNA data. Viral and bacterial taxonomic profiles were integrated to analyze interactions with treatment progression.

Results: An average of 4,750,000 reads were sequenced in each sample, with 6.5 ± 10.2% of reads significantly hitting our viral database. We identified 168 unique viral taxa, with the majority belonging to bacteriophages (Fig 1). A spike in parabacteroides phase was observed in three individuals and may suggest a phase-bacteria relationship. We compared taxa to those identified from our study of pediatric treatment-naïve CD mucosal biopsies (n=40) and found a moderate correlation of relative abundances of viral families between each cohort (rs = 0.49, p = 0.0096).

Conclusions: Our study is the first attempt at integrating viral MGS and 16S microbiome data in pediatric CD patients. This preliminary analysis warrants further work to gain insight into the bacteriophage-bacteria interaction during treatment.

Keywords: Crohn’s Disease, Gut Virome, Bacteriophage, Microbiome
**P045. Combination of oral antibiotic as a rescue therapy in pediatric inflammatory bowel disease: our experience**

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**Background:** Combination of oral antibiotics for Pediatric IBD involving the colon, has been proposed as a rescue therapy in refractory cases. The aim of the study is to review our experience with this strategy.

**Methods:** retrospective study based on the review of medical reports including all children with IBD who received as a rescue therapy a combination of oral antibiotics [Doxycycline (Ciprofloxacin for <8 years old), Metronidazole, Amoxicillin and Vancomycin]. Clinical and epidemiological variables were collected. The duration of the treatment and clinical response (by Pediatric Ulcerative Colitis Activity Index or Pediatric Crohn's Disease Activity Index) were evaluated at week 1, week 3 and week 12, and inflammatory markers (ESR, CRP) at baseline, week 1 and week 3.

**Results:** Six cases with moderate-severe refractory disease were included (5 Ulcerative Colitis, 1 colonic Crohn's disease). Median age was 11.5 years (IQR 5.3-13.6), with a median disease duration of 15 months (IQR 10-39). All of them were corticosteroid-dependent (N = 4) or resistant (N = 2). 4/6 patients were refractory to anti-TNF therapy (Infliximab). Median duration of treatment was 58 days (range 3-122 days). One of the patients was discontinued after 3 days due to clinical worsening. Clinical remission (PUCAI <10 or PCDAI <12.5) was achieved in 33% (N = 2) of the cases and response in 33% (N = 2) at 3 weeks of treatment. Inflammatory markers improved in 3/6 cases at week 1, and in 4/6 cases at week 3. At 12 weeks follow-up, 83% of the patients (n=5) needed a change of therapy.

**Conclusions:** Although the combination of oral antibiotics seems to be effective in the short term in some cases of refractory colonic IBD, this effect seems to be transient, requiring a different therapeutic strategy in the medium-term in most of our patients.

**Keywords:** Refractory PIBD, antibiotherapy

**P046. Thiopurines treatment in children with Inflammatory Bowel Disease: a survival analysis of the long term efficacy**

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**Background:** The efficacy of Thiopurines as treatment for prevention of relapses in Pediatric Crohn's Disease (CD) or Ulcerative colitis (UC) is still under debate. Although widely prescribed, the probability to continue treatment over time seems low.

**Objectives:** The primary objective was assessing the proportion of children with treatment failure. The secondary objectives were to evaluate: 1) the proportion of patients with Thiopurine Methyl Transferase (TPMT) deficiency; 2) the impact of 6-thioguanine (6TGN)/6-methyl-mercaptopurine (6MMP) ratio on treatment cessation; 3) the factors that could predict long-term response.

**Methods:** We identified all children exposed to Thiopurines within the first year of diagnosis in our IBD database. Data on diagnosis, disease location, time of initiation, dose and reason of cessation were extracted. We used Cox proportional hazard model to investigate the association between those variables and probability of Thiopurine cessation.

**Results:** 200 patients (53.5% females) were treated with Thiopurines (Azathioprine=150 (75.0%), Purinethol=50 (25.0%)). Median (IQR) time to initiation of therapy was 36.5 days (38.4). Before initiation, TPMT activity was assessed in 193 children; six (1.2%) patients among 512 tested had TPMT levels lower than 25 nmol/gHb/h. Thus, most patients started treatment with a median dose of 1.75 mg/kg for Azathioprine. Treatment cessation occurred in 137 children (68.5%) because of treatment failure (n= 104 (75.9%)); allergies (n= 3 (2.9%)) or pancreatitis (n=10 (7.30%)). Median duration of therapy was 13.7 months. Median 6TGN/6MMP ratio was 5.5 (8.9). No association was found between the following variables and treatment cessation: sex, age at diagnosis, disease type and early initiation.

**Conclusion:** Despite the promising results obtained by Markovitch et al. in 2000, the actual long term benefits of Thiopurines are low. We found that less than 50% of children maintained treatment after two years of follow-up. Reasons for treatment cessation were failure to maintain remission or adverse events.
P047. Reliability of Hematologic Indices for Monitoring Thiopurine Therapy in Pediatric Inflammatory Bowel Disease

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Introduction: Thiopurine medications (azathioprine and 6-mercaptopurine) have long been a mainstay of IBD therapy. 6-thioguanine (6-TGN) level is significantly associated with therapeutic response in IBD, but it is expensive and not universally available. Reports of hematologic indices, e.g., mean corpuscular volume (MCV), leucocyte count, and lymphocyte count as surrogate markers for 6-TGN levels have been controversial. Furthermore, their reliability in children is unclear.

Aims and Methods: A retrospective cross-sectional study. We analyzed 61 measurements of 38 children treated with thiopurines for IBD between November 2014 and February 2017. (1) analyzed the relationship between 6-TGN level and hematologic indices using Spearman’s rank correlation coefficient. (2) compared hematologic indices between the therapeutic level [6-TGN level > 235 pmol/8 × 10⁸ RBC] and sub-therapeutic level groups (6-TGN level < 235 pmol/8 × 10⁸ RBC). (3) determined the accuracy of macrocytosis (defined as MCV > 95 fl), leucopenia (<4.0 × 10⁹/l), and lymphopenia (<1.5 × 10⁹/l) for 6-TGN >235 pmol/8 × 10⁸ RBC. In referring to leucocyte count, cases used in combination with prednisolone were excluded.

Results: Of the 61 measurements, 80% UC and 20% CD. Combination with prednisolone was used in 17 (28%) children. A mild statistical significance was observed in Spearman’s rank correlation coefficient between 6-TGN levels and MCV (r = 0.259, p = 0.0588); however, no statistical significance between 6-TGN levels and any other hematologic indices. Between the therapeutic and sub-therapeutic level groups, we observed no significant differences in all hematologic indices. Macrocytosis was observed in only two cases, which 6-TGN level were <235 pmol/8 × 10⁸ RBC. Furthermore, leucopenia and lymphopenia were poorly predictive of therapeutic 6-TGN levels (each PPV and NPV were <70%).

Conclusion: We concluded that none of the evaluated hematologic indices is a reliable surrogate marker for 6-TGN levels in pediatric IBD.

P048. Epstein-Barr virus status and thiopurine therapy in pediatric IBD: a 20-year single centre experience

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Introduction: Infection with Epstein-Barr virus (EBV) in thiopurine (TP) treated patients represents a risk factor for developing severe complications, including lymphoproliferative diseases.

Aims: We aimed to describe EBV status in newly diagnosed IBD children and related complications, during TP therapy.

Methods: All IBD patients from our tertiary centre database (1998-2017) were reviewed. EBV serology (VCA Ig G and M) was recorded at diagnosis and during follow-up. STATA software version 13 was used for analysis.

Results: We diagnosed 96 patients (mean age ± SD at diagnosis 12.5±3.8 years, 59% male, 44 CD and 52 UC) belonging to 66% country. EBV was screened at diagnosis in 61% of patients and 76% were Ig G positive (69% CD, 88% UC, p=0.07). Before 2012, these tests were performed in 33% and as of 2012 in 90%, p<0.00001. Fifty nine patients (66% male) received TP for 132.75 patient-years. Before TP initiation, EBV status was documented in 79% (18% for suspicion of acute infection, 82% for screening, p=0.0035); seropositivity was found in 76% (89% CD, 63% UC, p=0.05). Eight (73% of EBV naïve patients) developed primary asymptomatic infection (7 CD, 5 male, none on biologics), at a mean of 14±11 months after initiating TP. No complications occurred in TP treated patients. No patient had to discontinue TP.

Conclusions: In this study representative for our country, of newly diagnosed patients, 61% were tested for EBV (79% before starting TP), with a significant increase since 2012 (90% of patients), following a strict protocol. The prevalence of EBV seropositivity at diagnosis in the total population was high (76%), as was before initiating TP, without significant difference between IBD subtypes. TP were associated with a high rate of primary EBV infection. No complications appeared, however decision on TP use in these patients should be reconsidered.

P049. Cyclosporin A efficacy in Pediatric ulcerative colitis- a retrospective single center study.

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Introduction: According to ECCO/ESPGHAN consensus for managing acute severe ulcerative colitis in children, Cyclosporin A remains a rescue therapy in acute steroid-refractory ulcerative colitis.

Aims: to assess a therapeutic efficacy of CsA in paediatric ulcerative colitis.

Materials and methods: It is a retrospective, single center study. We describe a clinical characteristic of 59 children (33F, 26M), mean age of 13,7 years, mean disease duration 32 months, who underwent CsA treatment in the course of UC in years 2005-2015. The primary endpoint was established as clinical remission (defined as PUCAI<10) or clinical response (defined as decrease in PUCAI scoring for at least 20 points) at Day 8 . The secondary endpoints were clinical remission/response at month 6 and colectomy rate. The clinical outcome was related to clinical (PUCAI score), laboratory (cholesterol, creatin level, CsA concentration), endoscopic (disease extension and severity) and demographic (age, age of onset, disease duration) data and previous anti-TNFalpha exposure.

Results: Short-term response/remission at Day 8 was achieved in 43 out of 59 (81%) and 31 out of 59 (58%) patients respectively. Long term remission evaluated in 6 month after therapy had been sustained in 19 out of 31 patients (63%). Colectomy rate was 15% (9/59). We observed no significant difference between groups with response/remission vs. no response/ remission at both analyzed timepoints in analyzed clinical, laboratory, endoscopic and demographic data. Previous anti-TNFalpha exposure did not affect clinical outcome.

Conclusion: CsA rescue therapy is effective in up to 80% of paediatric UC patients. 6 months remission is sustained in 32% patient. Colectomy rate is about 15%.

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Background and objectives: The efficacy of oral tacrolimus (TAC) as an induction therapy for ulcerative colitis (UC) has been demonstrated in adults. However, few data exist about pediatric UC. Furthermore, TAC is often used as a bridging therapy to thiopurines, so long-term outcome as a maintenance therapy is uncertain. We aimed to assess the short- and long-term outcomes and adverse events of oral TAC in children with UC.

Methods: We retrospectively assessed patients with steroid-dependent (SD) and steroid-refractory (SR) UC treated with oral TAC at Saitama Children’s Medical Center, between October 2011 and April 2017. Oral TAC was initiated 0.05-0.1mg/kg/day, and which was adjusted to achieve a trough level of 10-15ng/mL for induction, and 5-10ng/mL for remission. The primary and secondary outcomes were clinical remission (CR) in induction, long-term maintenance efficacy and adverse event, respectively.

Results: Seventeen patients received 18 TAC therapy inductions (including one patient receiving re-induction). The median observation period was 1.83 years (range: 0.5-8.5 years). The mean age was 13.0±3.5 years (range: 1.9-18.6 years). The patient with SD UC and those with SR UC had 9 inductions. The CR rate in induction was 77.8%. The mean time to CR was 11.2±5.0 days. The relapse-free survival rates were 85.7%, 57.1% and 50% at 12, 24, and 52 weeks, respectively. The median TAC maintenance duration was 374 days. Only one patient with SR UC achieved TAC-free remission, but 61.5% were switched to biologic agents. The colectomy rate was 17.6%. The adverse events were transient renal dysfunction (eGFR < 90) in 66.6% patients, hypomagnesemia (< 1.5mg/dL) in 83.3%, and tremor in 11.1%.

Conclusions: Oral TAC was effective as pediatric UC induction therapy. Nevertheless, more than half of the patients were switched to biologics during maintenance therapy. The long-term efficacy remains controversial considering its efficacy and renal side effect.

P051. Can early need of biologic therapy in patients treated with exclusive enteral nutrition be predicted at diagnosis?

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Background and objectives: Exclusive enteral nutrition (EEN) is effective to induce remission in mild-moderate Pediatric Crohn’s disease (P-CD). Early association with an immunomodulator for maintenance of remission is common. Our aim is to identify clinical or analytical factors at diagnosis predictive of early need of biological therapy.

Methods and Materials: Retrospective cohort study of P-CD patients treated at diagnosis with EEN and Azathioprine (AZA) (January 2015-August 2016). The cohort was divided into two groups depending on treatment at 6 months after diagnosis: group A (patients on monotherapy with AZA) and group B (patients on anti-TNF treatment).

Results: 25 patients were included. Group A included 14 patients (56%) and group B, 11 (44%) patients that had needed to step-up to anti-TNF (4 before ending EEN). Mean age at the beginning of symptoms in group B was statistically significant lower (p<0.05) compared with group A (10.8 vs 13.5), as well as the age at diagnosis (11.8 vs 13.8). There were no statistically significant differences on analytic parameters (hemoglobin, hematocrit) neither inflammatory markers (CRP, ESR, Fecal Calprotectin (FC)). Nevertheless, patients in group A had lower hemoglobin and hematocrit levels (10.8 vs 11.5 g/dL; 34.2% vs. 36%) and higher levels of CRP (56.1 vs 36.5 mg/L), ESR (32 vs. 21 mm/h) and FC (3200 vs 3071 mg/kg). PCDAI at diagnosis was slightly higher in group A (32.3 vs 27.7). The Waterloo index for weight at diagnosis showed worse nutritional status the patients on group A as compared with group B (83.3% vs 89.5%; p<0.05).

Conclusions: The early parameters in the study are not able to predict the need to start biological therapy in a short-mid time in this group of patients. Surprisingly, patients with higher inflammatory burden are more able to maintain remission with AZA. However, these differences are not statistically significant.

P052. Clinical and laboratory variables that predict clinical and endoscopic remission in children with Crohn's disease treated with infliximab

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Introduction: Repeated colonoscopies are impractical, especially in children relegating extreme importance to the validation of well-established, non-invasive measures of disease activity.

Aims: We aimed to identify early clinical and laboratory predictors of sustained clinical and endoscopic remission in children with Crohn’s disease (CD) under infliximab (IFX).

Materials and methods: Prospective study conducted in children with moderate-to-severe CD starting IFX treatment. All patients underwent endoscopy, weighted pediatric CD activity index (wPCDAI) assessment, C-reactive protein (CRP) at week 0 and 52. wPCDAI and CRP were also evaluated at 14 weeks. The primary outcome was to determine the ability of 14-week wPCDAI and CRP to predict steroid-free sustained remission and mucosal healing at 1 year. As a secondary outcome we sought to evaluate the concordance between wPCDAI and Simple Endoscopic Score for CD (SES-CD) at week 52.

Results: Forty-one children were enrolled (median age 13.5±2.7, females 41.5%). At 1 year, 21 (51%) and 16 (39%) were in clinical (wPCDAI <12.5) and endoscopic (SES-CD<3) remission, respectively. Fourteen-week wPCDAI didn’t differ between patients who achieved both clinical and endoscopic remission at 1 year (p=0.21 and p=0.35, respectively). By using a multivariable logistic regression model, neither week-14 wPCDAI nor CRP were predictors of 1-year clinical (p=0.83 and p=0.30, respectively) and endoscopic remission (p=0.22 and p=0.48). wPCDAI resulted significantly correlated with 1-year SES-CD (r=0.38, p=0.01). The concordance between wPCDAI and SES-CD was excellent and good for severe disease and remission (k cohen 0.87 and 0.76), moderate and absent for mild and moderate disease, respectively.
Conclusions: Based on our results, 14-week post induction wPCDAI and CRP are not predictors of 1-year sustained steroid-free clinical and endoscopic remission in children with CD under biologic therapy. Continuous wPCDAI shows a good correlation with SES-CD, particularly for patients in remission and with severe disease.

P053. Clinical course after induction therapy with infliximab in pediatric patients with inflammatory bowel disease

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Background: Infliximab has modified treatment strategies and disease course of pediatric inflammatory bowel disease (IBD).

Objective: To characterize clinical course in children with IBD after induction therapy with infliximab.

Methods: Retrospective analysis of IBD patients under infliximab therapy for a minimum 6 months period between 2010 and 2016.

Results: Sixty patients were included. Eighty two percent had Crohn’s disease, 65% were male and the median age was 16 years. There were 42 patients under treatment with infliximab for 12 months, 24 patients for 2 years, and 11 for 3 years. Switch to an alternative biological agent or suspension of biological therapy occurred in 17.2%. At the time of the first infusion, disease activity was classified as mild in 68%, moderate in 17% and severe in 7%. Median fecal calprotectin (FC) was 792 mcg/g, median sedimentation rate (SR) was 28 mm and median C-reactive protein (CRP) was 12.7 mg/L. Following induction therapy, 73% (44/60) achieved remission. At that time, median values for FC, SR and CPR were 278 mcg/g, 10mm and 1mg/L, respectively. Remission was achieved in 70% (42/60) of patients at 6 months of infliximab therapy, in 76% (32/42) at 12 months, in 67% (16/24) at 2 years and in 82% (9/11) at 3 years. Attaining remission after induction therapy was associated with maintaining remission at 6 and 12 months (p = 0.041, p = 0.040). This difference is not evident at 2 and 3 years of treatment. Eighty seven percent of patients were under combination therapy with a thiopurine. Combination therapy was not associated with disease remission at 12 months, 2 or 3 years. There was no association between this practice and switch of biological agent or suspension of biologic therapy.

Conclusions: Obtaining remission after induction therapy with infliximab was associated with maintenance of remission at the first year of treatment.

P054. The results of 1 year infliximab treatment in children with Crohn’s disease—the PIT-STOP study

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Introduction: The anti-tumor necrosis factor alpha therapy was available for pediatric patients with Crohn’s disease since 2007 March in Hungary. The biological therapy has a big impact on achieving the steroid-free long term remission. The infliximab, which was the first and chimeric antibody financed for a one-year period by the health insurance. According to the studies done in adult population, the relapse rate after one-year infliximab treatment is between 43.9% and 45% (STORI and RASH studies). These data suggest the importance of the continuation of the biological therapy after the one-year period.

Aims: Therefore we started a multicentre retrospective study in 2015 to investigate the relapse rate and time to relapse as a primer end-point along with the risk factors of it (PITSTOP – Pediatric Infliximab Treatment Stop).

Methods: Pediatric patients were enrolled with one-year follow-up time after one-year infliximab therapy regardless of whether the anti-tumor necrosis factor alpha therapy needed to be restarted or not.

Results: 99 children (53 boys, median age [interquartile range] 13.1 [11-14.7] years) were recruited from the seven biggest Hungarian IBD centrum. The disease duration between the diagnosis and the biological therapy introduction was 1.7 [0.9-3.3] years. The infliximab therapy was restarted during the one-year follow-up period in 55.4% of patients after 0.8 [0.3-1.0] year. Risk factor for the reintroduction was the steroid-need during the initiation of infliximab therapy at the beginning (OR 2.940 [1.160-7.452] - p=0.023). However the metronidazole therapy at the time of diagnosis was a protective factor (OR 0.289 [0.095-0.838], p=0.0029).

Conclusions: These data are in line with that from adult population and suggest the importance of the continuation of infliximab therapy after one-year.

P055. Infliximab in pediatric inflammatory bowel disease: maintaining or changing the therapy

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Background and objectives: Infliximab reshaped the therapeutic intervention in inflammatory bowel disease (IBD). We aimed to analyze children that initiated infliximab and characterize the clinical course during the following three years of therapy.

Methods: Retrospective observational study of all children with IBD who underwent infliximab, in a Pediatric Gastroenterology Unit, between 2010 and 2016.

Results: Sixty-seven individuals were included, 66% male, with a median age (minimum-maximum) of 16 (9-19) years and a median follow-up of 31 (5-115) months. In Crohn’s disease (n=52), infliximab was initiated 11 (0-67) months after diagnosis; 29% were previously non-responsive to conventional therapy; 3 patients started infliximab at the time of diagnosis (2 with severe perianal disease and 1 with uveitis). In those with Ulcerative colitis (n=15), infliximab was initiated 11 (0-70) months after diagnosis; 73% presented corticosteroid/corticoiddependent disease and 1 patient initiated it at the time of diagnosis with severe disease. Thirty-four patients (61%) adjusted the dose/frequency of infliximab at 8 (1-26) months. In 46 (69%) children, remission was achieved at the end of the induction phase. In the other cases, 9 adjusted the dose/frequency of infliximab and, of these, 5 didn’t obtained remission at 6 and 12 months. Bowel resection was performed in 5 (8%) cases. Eight (12%) cases required the change of the biological therapy (1 anaphylaxis and 7 primary failure of infliximab).
Conclusions: In pediatric IBD, the treatment with a biological agent may be justified at the time of diagnosis. The need to adjust dose / frequency often occurs during the first year of treatment. The absence of remission in the induction phase anticipates a probable need of therapeutic change and the alteration of biological agent should be considered. Serum drug and antibody levels may help to support this decision.

**P056. Out of Window Infliximab Infusions Do Not Drive Loss of Response or Low Trough Drug Levels**

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Background and objectives: There is a growing body of literature demonstrating that sustained clinical remission using infliximab is related to adequate trough serum drug levels and inversely to the development of antibodies against the drug. Although there is little literature reviewing the outcomes of patients with respect to adherence to scheduled dosing intervals, it stands to reason that patients who repeatedly receive their infusion outside of the intended treatment window, especially when given late, may be at greater risk of low drug levels & loss of response to therapy.

Methods: A retrospective analysis of patients receiving infliximab in the Edmonton Pediatric IBD Clinic (EPIC) was performed and the difference between scheduled and actual infusion was calculated to determine who fell outside the intended window. Pearson correlations were calculated for dose or frequency escalation and dosing interval adherence.

Results: Data from 121 patients receiving infliximab was analyzed. There were 1991 individual infusions (394 induction doses, 38 re-inductions following loss of response and 1559 maintenance doses). The median dose interval discrepancy was 0 with a range of -27 days to +26 days (mean -0.189, SD 3.48 days). 265 maintenance doses (18%) were received out of window (129 >3 days of intended date, 156 <3 days). There were 8 cases of loss of response to infliximab (increased disease activity scores) and 28 cases of infliximab escalation (loss of response or low trough levels measured as part of routine monitoring), neither of which correlated with out of window infusions (r=0.47; r=0.39).

Conclusions: 82% of infliximab infusions were administered within an acceptable time window of the prescribed frequency. Of those patients who had a clinical loss of response or who had measured infliximab trough levels <3, out of window infusions appear to play no significant role.

Keywords: Inflammatory bowel disease, infliximab, loss of response

**P057. Individualised Infliximab treatment guided by patient-managed eHealth in children and adolescents with IBD**

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OBJECTIVES AND STUDY: The aim was to individualise the timing of infliximab (IFX) treatment in children and adolescents with IBD using a patient-managed eHealth solution.

METHODS: IBD patients, 10-17 years old, in ongoing IFX treatment, were prospectively included in an open label intervention study. Patients used the eHealth homepage www.young.constant-care.com. The disease burden was estimated weekly by a combination of patient-reported symptom score and faecal calprotectin (FC) level starting four weeks after the last infusion. The IFX-infusions were given with 4-12 weeks intervals and the weekly calculated disease burden determined the timing for the next infusion. Treatment intervals, trough levels of IFX concentration and antibodies were compared with a control group (standard IFX treatment).

Patients and their parents evaluated the eHealth program. RESULTS: 50 patients were included (29 eHealth; 21 control). 95 infusions were provided in the eHealth group (mean interval 9.5 weeks, SD 2.3), and 105 infusions in the control group (mean interval 6.9 weeks; SD 1.4). We found significant longer treatment intervals in the eHealth compared with the control group (Mixed Effect Model: P< 0.001). Treatment intervals pr. patient altered during the eHealth participation. Number of patients developing antibodies against IFX was not significant different comparing the eHealth and control group (Fisher’s exact test: P=0.24). The overall adherence to the eHealth program was 74% regarding the electronic entries of symptoms (827 out of 1123 expected) and 72% regarding FC samples (804 out of 1123 scheduled). None of patients or parents felt unsafe using the eHealth program. 80 % of the patients (86 % parents) reported increased control of the disease, and 63% reported better knowledge about her/his disease.

CONCLUSION: Self-managed eHealth facilitated individualised timing of IFX treatments within treatment intervals of 4-12 weeks. Patient’s eHealth performance was acceptable. Patients reported better control and improved knowledge of their IBD.

**P058. Proactive approach of therapeutic drug monitoring (TDM) in Pediatric Inflammatory Bowel Disease (PIBD) on maintenance biologic treatment improves clinical remission**

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Background and Aim: Infliximab (IFX)/Adalimumab (Ada) are used as maintenance therapy in PIBD. There is reactive or proactive approach to TDM. We looked at trough levels of IFX/Ada, presence of ADA and correlation to clinical response. Methods: We conducted a retrospective study (n = 67, Crohn’s disease [CD] = 47, ulcerative colitis [UC] = 11, inflammatory disease unclassified [IBDU] = 7) and Early onset IBD [EOIBD] = 2); Male n=43, age range 4 years 3 months-17y; median 13y8m). 42 patients were on IFX only, 25 on Ada. Results Group 1 IFX converted to Ada; n=25 patients; CD n=15, UC n=3, IBDU n=5, EOIBD n= 2. Lowest Ada trough levels n=2; median 5.6, range 0.3-17; highest median 9.1, range 3.7-12.7. ADA for Ada negative in 16 patients, n=5 positive over time, n=2 positive at first measurement. Group 2 IFX only; n=42; lowest IFX through levels, median of 1.4, range <0.8-32.5, highest trough levels median 5.2, range 0-45. ADA for IFX
negative in n=37, n=7 developed antibodies, median ADA of 61, range 10>200. 50 % (21/42) of patients received double doses. 5 patients were given 15mg/kg. In 81 % (17/21) of patients, double dosing led to an incremented of trough levels above >2, median 4.1, range 2.4-21.9. 15/67 (22%) out of 67 patients had completely normal laboratory tests, 42/47 (89%) CD patients had normal PCDAl, 10/19 (91%) UC patients had normal PUCAI. 14/47 (30%) CD patients developed antibodies to IFX, 2/11 (18%) UC patients developed antibodies to IFX. Conclusion The vast majority of patients on IFX/Ada had an excellent clinical response with this proactive approach, thus enabling us to optimize treatment and bring them into clinical remission. We advocate proactive biologic drug monitoring.

P059. Association between infliximab trough levels, antibodies to infliximab and clinical remission in pediatric patients with inflammatory bowel diseases

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Introduction: Pediatric data on Infliximab serum trough levels (IFX-TL) and antibodies to Infliximab (ATI) is scarce. We aimed to longitudinally evaluate the association between IFX-TL, ATI and disease activity in children with IBD.

Subjects and Method: A retrospective cohort of children (42 CD, 12 UC, 2 IBD-U), treated with IFX between Jan 2011 and Dec 2016 was performed. Demographic and clinical data were retrieved from medical charts. Disease activity was evaluated at each visit by the Harvey Bradshaw Index (HBI) for CD, PUCAI for UC and physician global assessment (FGA) for both, and CRP level was measured.

Results: A total of 668 samples, obtained at trough during induction (n=64; 9.6%) and maintenance (no=604; 90.4%) periods, were analyzed. CRP level was available in 62.8% (n=420). Median IFX-TLs were significantly higher in patients with clinical remission than in those with active disease (5.27 vs. 4.27 μg/ml, p = 0.032), and ATI levels were higher among clinically active patients (2.48 vs 1.58 μg/ml, p=0.0005). Elevated CRP was associated with higher ATI levels (2.62 versus 1.76 μg/ml, p =0.021), but not with IFX-TLs (p = 0.68). Week 2 median IFX-TLs (28 patients) were higher and ATI levels were lower for patients in remission at weeks 14 (p = 0.44 and 0.13, respectively) and 22 (p=0.55 and 0.87, respectively), than in those with active disease.

Conclusion: Serum IFX-TL and ATI were associated with disease activity, but week 2 IFX-TL were not predictive of remission at week 14 and 24, in children with IBD. This lack of predictive effect may be a result of a small cohort of patients. As shown in previous studies, concomitant immunomodulator therapy was significantly associated with remission rate.

P060. Post-induction serum infliximab trough levels are capable of predicting 'en bloc' remission in pediatric Crohn's disease patients under combined immunosuppression

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Introduction: Early infliximab (IFX) trough level (TLs) at week 14 are associated with persistent remission throughout week 54 in pediatric patients with inflammatory bowel disease (IBD). However, there is limited data regarding the association between IFX TLs at week 14 and mucosal healing (MH) in pediatric IBD.

Aims: To investigate whether IFX TLs at week 14 (TL14) were associated with MH at week 14 (MH14) and week 54 (MH54) and with 'en bloc' remission, a composite outcome of clinical, biochemical, and endoscopic remission throughout the period, in pediatric CD patients.

Materials and Methods: We performed a retrospective study in 64 patient with pediatric CD under combined immunosuppression with IFX and azathioprine, who had measured TL14, and had conducted ileocolonoscopies at week 14 and 54. MH was defined as SES-CD=0. 'En bloc' remission was defined as MH at both week 14 and 54 plus persistent clinical and biochemical remission from week 14 to 54 in the absence of dose intensification.

Results: MH14 and MH54 was achieved in 28 (43.8%) and 40 patients (62.5%), respectively. 'En bloc' remission was observed in 18 patients (28.1%). TL14 were significantly higher in patients who had each achieved MH14 (median 6.0 vs. 3.0 μg/mL, p<0.001), MH54 (median 4.9 vs. 2.5 μg/mL, p<0.001), and 'en bloc' remission (median 6.2 vs. 3.4 μg/mL, p<0.001). According to logistic regression analysis, TL14 was significantly associated with MH14 (OR=1.40, 95% CI=[1.13-1.83, p=0.006], MH54 (OR=1.82, 95% CI=[1.35-2.64, p<0.001), and 'en bloc' remission (OR=1.33, 95% CI=1.09-2.72, p=0.015). According to ROC curve analysis, the best cut-off value of TL14 required in achieving MH14, MH54, and 'en bloc' remission were 4.49, 4.01, and 4.81 μg/mL, respectively.

Conclusions

TL14 were associated with each MH14, MH54, and 'en bloc' remission. Post-induction IFX TLs are capable of predicting 'en bloc' remission, a novel composite remission outcome.

P061. Clinical utility of therapeutic drug monitoring in predicting mucosal healing in pediatric Crohn's disease patients under maintenance infliximab treatment

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Introduction: There is limited data regarding the association between serum infliximab trough levels (TLs) and mucosal healing (MH) in the pediatric population of Crohn's disease (CD).

Aims: To investigate whether serum infliximab TLs were associated with MH and to identify the cut-off level required for MH in pediatric CD patients under maintenance infliximab treatment.
Materials and Methods: We conducted a single center, retrospective cross-sectional study of 105 patients with pediatric CD who had been receiving infliximab for at least 1 year. MH was defined as a Simple Endoscopic Score for Crohn’s disease (SES-CD) of 0. Logistic regression analyses were performed to examine the association between demographic, clinical, biological variables including serum infliximab TLs and MH. Receiver operator characteristic curves were used to derive the cut-offs of serum infliximab TLs required to achieve MH.

Results: The median duration of infliximab treatment was 1.0 year (range 1.0-3.2 years), and MH was achieved in 49% (51/105). Median serum infliximab TLs were significantly higher in patients with MH compared to those without MH (median 4.5 vs. 3.3 µg/mL, p=0.002). According to multivariate logistic regression analysis with stepwise selection, infliximab TL along with B1 behavior and the duration from diagnosis to infliximab were significantly associated with MH (OR=1.479, 95% CI=1.176-1.86, p<0.001; OR=3.524, 95% CI=1.061-11.701, p=0.04; OR=0.529, 95% CI=0.344-0.813, p=0.004, respectively). The most accurate cut-off of infliximab TL in identifying MH was 4.2 µg/mL (AUC=0.679, 95% CI: 0.576-0.782, p<0.001), while the cut-point for a specificity of 80% was 5 µg/mL (sensitivity 39%, specificity 80%, PPV 65%, NPV 58%).

Conclusions: There was a significant association between serum infliximab TLs and MH in pediatric CD patients under maintenance infliximab. In order to achieve MH in over 80% of pediatric CD patients during infliximab maintenance, an infliximab TL of ≥5.0 µg/mL is required.

P062. Combination therapy with methotrexate does not appear to change infliximab trough levels nor anti-infliximab antibodies in children

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Introduction: Debate remains regarding the risks/benefits of infliximab monotherapy vs. combination therapy with methotrexate.

Aims: This prospective cross-sectional study assessed the impact of methotrexate on infliximab troughs and anti-infliximab antibodies in children.

Materials/Methods: Serum infliximab troughs and anti-infliximab concentrations were measured (NF-kB luciferase gene-reporter assay; ARUP Laboratories) in 50 children (6-21 years old), receiving infliximab for IBD (n=41; 82%) or juvenile idiopathic arthritis (JIA). Children who received <14 weeks of infliximab, had dose or dose-interval adjustments during the previous 2 infusions, were excluded. For children receiving concomitant methotrexate therapy (n=18), dose-for-weight-adjusted erythrocyte methotrexate-polyglutamates concentrations were determined via validated HPLC-MS/MS methodologies, to account for known variability in methotrexate drug disposition. Anti-infliximab concentrations and infliximab troughs, unadjusted and adjusted for dose-per-kilogram, were compared via independent student t-test in children receiving monotherapy vs. combo-therapy. Relationships between infliximab and methotrexate-polyglutamates levels, dosing intervals, patient demographics and disease specifics were explored via Spearman’s correlation (r₂).

All statistical analyses were performed using SPSS v23; α<0.05.

Results: Infliximab troughs were comparable in children receiving monotherapy vs. combo-therapy (15.3±13.2 vs. 20.5±15.6 µg/ml), as were troughs adjusted for mg/kg infliximab received (1.73±1.58 vs. 1.64±1.54 µg/ml); p=0.5. No statistical differences in age, ESR, CRP or albumin were observed between children receiving monotherapy vs. combo-therapy. Higher methotrexate-polyglutamates concentrations were not associated with higher infliximab troughs (r₂=-0.065; p=0.69). Of the 2 children (4%) with detectable anti-infliximab concentrations, one received monotherapy, one combo-therapy. Both had IBD and undetectable troughs. Of the 3 children (6%) with undetectable troughs, all had IBD: one with quiescent, one with mild and one with moderate disease (PGA).

Conclusions: Combination therapy with methotrexate does not appear to affect serum infliximab troughs nor anti-infliximab antibodies in children. Higher methotrexate-polyglutamates concentrations did not correlate with higher infliximab troughs, suggesting that lack of methotrexate effect on infliximab pharmacokinetics is not dose-dependent.


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Background and objectives: No data are available on the effect of CT-P13, the first biosimilar infliximab, on mucosal healing (MH) in Crohn disease (CD). Our aim was to evaluate the efficacy of CT-P13 therapy on remission rate and MH in a cohort of paediatric CD patients.

Methods: Biologic naïve, 33 CD patients, who started CT-P13 therapy were consecutively enrolled in a prospective study. Demographic data, medical treatment, and laboratory results were documented. Weight Paediatric Crohn Disease Activity Index (wPCDAI) was used for evaluation clinical activity, and Simple Endoscopic Score (SES-CD) for mucosal healing, performed before CT-P13 therapy (T0) and after the 3rd dose at week 10. Clinical remission was defined as wPCDAI ≤12.5, MH as SES-CD ≤2, partial MH as a reduction of 50% in SES-CD from T0, and no endoscopic healing as no variation or worsening of the SES-CD.

Results: At the enrolment, 26/33 patients were diagnosed with luminal, 4/33 with complicated and 3/33 with perianal disease. All but one patients presented active disease by wPCDAI, 7/33 mild and 25/33 moderate to severe disease activity. Indications for therapy were: refractory severe exacerbation (2/33), chronic refractory activity (22/33), tiopurine intolerance (3/33), steroids dependency (2/33), complicated disease, and perianal disease (3/33). Clinical remission was achieved by 81% patients. At week 10, there was a significant decrease in mean wPCDAI (51.8 ±9.4 to 9.0±5.3; P<0.01). One patient was considered as primary no responder. Complete and partial MH was achieved by 31% and 38% of patients, respectively, while 16% patients presented no or worsening of SES-CD. Median SES-CD was reduced from 13.6±7.8 to 6.33±5.55. One patient was considered as primary no responder.

Conclusions: CT-P13 was effective for induction of remission and MH in paediatric biologic naïve CD patients. The rates was similar to the historical studies with reference infliximab.

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Introduction: Adalimumab is an anti-tumor necrosis factor (ATNF) agent approved by the US FDA for pediatric Crohn’s disease in 2014. Aims: We assessed the duration and effectiveness of adalimumab treatment in pediatric Crohn’s disease patients without prior ATNF therapy.

Material and Methods: In a retrospective cohort study from 43 centers in the USA in the ImproveCareNow Network, ATNF-naïve patients induced with adalimumab prior to 18 years old with at least one post-induction visit were identified. We assessed the duration of treatment and the clinical effectiveness of adalimumab based on steroid-free clinical remission using Physician Global Assessment (PGA, inactive) and Short Pediatric Crohn’s Disease Activity Index (sPCDAI, ≤10). Clinical care and frequency of visits were decided by the patient, parent and clinician. Data from clinical care visits were assessed every 3 +/- 1.5 months for 1 year, then every 6 +/- 3 months through 3 years. Descriptive statistics, Fisher’s Exact Test and multivariable logistic regression analyses were performed.

Results: There were 174 patients treated with adalimumab (Table 1). The number of patients followed post-induction for 3, 6, 12, 24 and 36 months was: 174, 174, 154, 71 and 39; the percentage of followed patients remaining on adalimumab was: 100%, 95%, 94%, 97% and 80% (Table 2). Of patients on adalimumab at 3, 6, 12 and 24 months: 69%, 75%, 79%, 94% and 81% were in steroid-free clinical remission by PGA; and 71%, 77%, 80%, 91% and 86% by sPCDAI. Concomitant immunomodulator therapy did not appear to improve outcomes.

Conclusions: In the largest series with the longest follow-up, adalimumab was durable and effective as initial ATNF therapy for pediatric Crohn’s disease. Of patients followed for 24 months, 97% remained on adalimumab. Steroid-free clinical remission was achieved in 91% - 94% of patients who remained on adalimumab for 24 months.
P065 Efficacy of first line top-down adalimumab therapy

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Objectives: Anti-TNF agents are highly efficient in inducing and maintaining remission in pediatric Crohn's disease (CD) patients. An important question is when to start anti-TNF medication? The aim of our study was to compare two different strategies using either Adalimumab (ADA) in immunomodulator and anti-TNF naïf CD patients or in patients failing immunosuppressant therapy.

Methods: Pediatric patients followed for CD (onset <18 years) at Necker that initiated their ADA therapy between 2005 and 2017 were retrospectively reviewed. The beginning of the study (M0) is the date of first ADA injection. Enrolled patients were divided into 2 groups according to the treatment strategy used. Group A is composed of patients naïf of immunosuppressors and anti-TNF agents who started early ADA after induction of remission (top down strategy). Patients who started ADA in a step up manner after failure of immunomodulators (AZA and/or infliximab) were designated to group B. For each patient were collected clinical and biological data at M0, M3, M6 and M12.

Results: 82 patients (43 boys) were enrolled in the study, 44% (n=36) in group A and 56% (n=46) in group B. Mean age at diagnosis was 12.1 ± 2.7 years. At inclusion, the 2 groups were comparable. At M6, 24/30 (80%) of patients in group A were in steroid-free clinical remission (wPCDAI < 10) versus 35/39 (89%) of patients in group B and at M12, 20/23 (87%) and 30/35 (86%) in A versus B, respectively (NS). There was no significant difference regarding the biological parameters between the groups at 1 year follow up.

Conclusion: The present study demonstrates that a ”Top down” strategy with Adalimumab monotherapy early in disease course is highly effective in pediatric CD patients to maintain clinical and biological remission at 1 year and as effective as step-up combotherapy.

Keywords: Adalimumab, Crohn’s disease, strategy

P066. Potential utility of therapeutic drug monitoring of adalimumab in predicting short-term endoscopic and histologic remission in pediatric Crohn’s disease patients

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Introduction: There is limited data regarding mucosal healing (MH) and therapeutic drug monitoring in pediatric Crohn’s disease (CD) patients under adalimumab (ADL) treatment.

Aims: We aimed to investigate the association between ADL trough levels (TLs) and MH, and between ADL TLs and histologic remission (HR) at 4 months from ADL treatment in the pediatric population of CD.

Material and Methods: This study was a preliminary study of an ongoing prospective cohort in pediatric CD patients receiving ADL at the Department of Pediatrics, Samsung Medical Center. Moderate-to-severe luminal CD patients who were naïve to biologics were included. Ileocolonoscopies and biopsies as well as clinical activity assessment, laboratory exams, including tests for ADL TLs and antibody to adalimumab (ATA) were performed at 4 months from ADL initiation. MH was defined as SES-CD=0. HR was defined as the complete absence of microscopic inflammation. ADL TLs and ATA status was compared according to MH status at 4 months.

Results: Seventeen subjects (13 males, 4 females) were included. At 4 months from ADL initiation, 14 patients (82.4%) were under clinical remission, 8 patients (47.1%) had achieved MH, and 4 patients (23.5%) had achieved HR. ADL TLs were significantly higher in patients who achieved MH compared to those who did not (13.0±6.5 vs. 6.2±2.6 μg/mL, p=0.023), and also significantly higher in patients who achieved HR compared to those who did not (17.9±5.3 vs. 6.8±2.5 μg/mL, p=0.02) (Fig. 1). ATA was detected in 1 patient (5.9%). According to ROC curve analysis, the optimal cut-point for predicting MH was 8.76 μg/mL.

Conclusions: Serum ADL TLs at 4 months were significantly higher in pediatric CD patients under MH or HR, compared to those who failed to achieve each outcome. Therapeutic drug monitoring may guide in determining short-term MH and HR in the era of treat-to-target.

P067. Evolution of the anti-Tnf trough levels after withdrawal of thiopurines in pediatric ibd patients on combination therapy

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Introduction: Combination Therapy (CT) with monoclonal antibodies against tumor necrosis factor alpha (anti-TNFα) and thiopurines has been proved to be effective for induction and maintenance of remission in pediatric IBD (PiBD) patients although this strategy is not free of potential side-effects. There is no consensus on the risk-benefit ratio of prolonged use of CT.

Aims: to report the evolution of serum anti-TNFα trough levels (ATR) after discontinuation of immunosuppressive therapy in PiBD patients previously treated with CT.

Material and Methods: Descriptive, retrospective study based on the review of medical records. PiBD patients on CT with azathioprine (AZA) and Adalimumab (ADA) or Infliximab (IFX), in clinical and endoscopic remission, with ATR in therapeutic ranges and negative antibodies against anti-TNFα, who discontinued immunosuppressive treatment were recruited. Evolution of ATR, appearance of immunogenic reactions and loss of response, as well as their correlation with clinical evolution, were analyzed at 3, 6 and 12 months of follow-up.

Results: We included 13 patients (5 women, 10 Crohn’s disease, 3 ulcerative colitis), mean age at diagnosis 10.2 years. After an average of 22.4 months of CT, AZA was stopped. All of whom completed follow-up at 3, 6 and 12 months 13/13, 9/13 and 4/13 patients respectively, remained in clinical remission. All of whom ATR results were obtained, at 3, 6 and 12 months 10/13, 3/9 and 3/4 patients respectively, therapeutic ATR were observed. A single patient had undetectable levels and positive antibodies despite being in clinical remission. None symptoms suggestive of drugs immunogenicity was observed.
Conclusions: The withdrawal of immunosuppressive therapy in PIBD patients on CT in clinical and endoscopic remission, with therapeutic ATR, did not lead to clinical changes in the short term in our cohort, although drug levels monitoring could contribute to the prevention of subsequent onset of immunogenicity and secondary loss of response.

P068. The local survey: use of biological therapies in pediatric IBD patients in Spain

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Background and objectives: Despite the recent publications on the use of biologicals (infliximab and adalimumab) in pediatric IBD, there are some issues still poorly defined. Our objective was to know the opinion of the different doctors who treat these patients in our country.

Methods: A questionnaire with 126 items was distributed to SEGHNP members through the mailing list.

Results: We received responses from 67 pediatric Gastroenterology Units. 86.8% had used these drugs in CD and 71.6% in UC. Regarding on safety, 27.9% and 33.9% believe in an increasing risk of infections or cancer, however, only 3.4% and 1.7% had observed it on their patients. 87% think that biological use in early stages can be beneficial, however, the 2 main reasons to not use them were: reserve this medication for future treatments (60.6%) and the risk of developing tumors (43.9%). Regarding on efficacy, evaluating primary response, 74.6% used calprotectin, 44.8% endoscopy, 22.4% MR enterography and 20.3% ultrasonography.

There is a consensus in indicating biologicals: persistent symptoms, corticosteroid dependency despite immunomodulators, corticoresistance and in complex, stenosing or/and fistulizing perianal forms in CD. The two factors that most influence the choice between the two drugs are: patient preference (83.1% in CD and 54% in UC) and the degree of compliance expected (89.8% in CD and 73.2% in UC). Regarding the practical management, 53.4% used premedication and 55.2% underwent endoscopic examinations to assess remission. Less than 40% of centers have anti-TNF a drug levels and antibodies.

Conclusions: Biologicals are widely used in pediatric IBD in Spain. Although they are recognized to have a potentially greater therapeutic benefit in the early stages of the disease, the major limitation in their prescription is to avoid an early exhaustion. There is wide variability in indications, response assessment, premedication and maintenance schedule.

Keywords: survey, biologicals, safety and efficacy

P069. Presence and severity of ulcerations in Crohn Disease does not contribute to response for induction therapy with infliximab in children

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Objectives: Induction therapy with infliximab is efficient in approximately 80% of children with Crohn disease (CD). It's documented that male sex, concurrent immunomodulators, non-smoking behavior and luminal disease are the predictors of good infliximab response. It is questionable if presence of colonic and ileal ulcerations can contribute response for biological therapy.

Aim: The aim of the study was to explore the contribution of presence and severity of ulcerations to response for induction therapy with infliximab in children.

Patients and Methods: This is a subanalysis of CIMIT study (JPGN: May 2015 - Volume 60 - Issue 5 - p 580–585). 99 patients with PCDAI>30 pts and endoscopic evaluation with SES-CD, based on 4 endoscopic variables (ulcer size, ulcerated and affected surfaces, stenosis) in 5 ileocolonic segments and the endoscopic parameters are scored from 0–3) performed were involved to the study and received induction therapy with infliximab 5 mg/kg at weeks 0, 2, and 6. Clinical (PCDAI score) response (decrease of PCDAI≥15 AND PCDAI<30) and remission (PCDAI<10) were assessed at Week 10. Scorings of ulcer size and ulcerated surface were used as two independent variables in analysis of discrimination between: group with clinical response vs. no response and group with clinical remission vs. no remission.

Results: None of the analyzed variable had significant impact on discrimination between group with clinical response vs. no response – all partial Wilks’ Lambda > 0.99. The optimal model of discrimination had sensitivity 1.00 and specificity 0.00. None of the analyzed variable had significant impact on discrimination between group with clinical remission vs. no remission – all partial Wilks’ Lambda > 0.99. The optimal model of discrimination had sensitivity 1.00 and specificity 0.00.

Conclusions: Presence and severity of colonic and ileal ulcerations in Crohn Disease does not contribute to response for induction therapy with infliximab in children.

P070. Presence and severity of ulcerations in Crohn's Disease contribute to the course of maintenance therapy with infliximab in children

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Objectives: The primary and secondary loss of efficacy are problems during antiTNF-α maintenance therapy. Complete remission, concurrent immunomodulators are the predictors of prolonged remission. It is questionable if presence of colonic and ileal ulcerations can contribute the CD flare.

Aim: The aim was to explore the contribution of presence and severity of ulcerations to the course of maintenance therapy with infliximab in children.

Patients and Methods: This is a per protocol subanalysis of CIMIT study. 77 patients with PCDAI>30 pts and endoscopic evaluation using SES-CD, based on 4 endoscopic variables (ulcer size, ulcerated and affected surfaces, stenosis) in 5 ileocolonic and the endoscopic parameters are scored from 0–3) performed before and after induction therapy, who finished one year maintenance therapy (infliximab5mg/kg) were involved. Clinical (PCDAI) remission (PCDAI<10) were assessed at Week 52. Scorings of ulcer size and ulcerated surface at Week 0 and Week 10 were used as independent variables in analysis of discrimination between: groups with clinical remission (with or without rescue therapy n=57) vs. no remission (n=20) and groups with CD flare present (n=34) vs. absent (n=43).

Results: None of the analyzed variable had significant impact on discrimination between group with clinical remission vs. no remission – all partial Wilks’ Lambda > 0.98. The optimal model of discrimination had sensitivity 0.98 and specificity 0.15.Ulcer size scoring at Week 0 had significant impact on discrimination between group
P071. Therapeutic drug monitoring during infliximab induction in Pediatric IBD: a multicentre prospective cohort study

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Background and objectives: Whilst therapeutic drug monitoring (TDM) is used during maintenance infliximab (IFX) therapy to assess loss of response and optimize regimens, desired IFX levels during induction have only recently been examined and only in adults*. Among pediatric IBD patients starting IFX, we measured drug levels prior to 3rd induction and 1st maintenance doses, aiming to determine the optimal dose level required to achieve target IFX levels at the start of maintenance.

Methods: Within the inception cohort study of the Canadian Children IBD Network, children initiating IFX had trough levels measured by ELISA at the time of final induction and first maintenance infusions. Influence of patient demographics and baseline clinical disease activity on early trough levels was assessed.

Results: From May 2016 - April 2017 at 9 participating sites, 109 children (median age 10.6 years, 55% male, 52% CD, 48% UC/IBD-U) were included. Induction regimen was “standard” (0,2, 6 weeks) in 78% and “intensified” in 22% (O,1, 4 weeks). As shown, IFX levels were highly variable prior to 3rd induction dose. Despite higher dosing per kg during induction and shorter interval to dose 4 in the intensified regimen, IFX levels at the start of maintenance were comparable to patients receiving standard induction. Baseline characteristics at initiation of induction, hemoglobin, albumin and disease activity predicted pre dose 3 trough levels (r² 0.8, p<0.001). In the standard group, we found that TDM at dose 3 was predictive of TDM at dose 4 (r 0.56, p <0.01).

Conclusions: Variability in infliximab exposure is evident during induction. Baseline factors at first induction dose predict infliximab exposure at subsequent doses. TDM holds promise at dose 3 in predicting levels during maintenance therapy.

Keywords: infliximab, induction, therapeutic drug monitoring.


P072. Anti-TNFα treatment following surgical resection for Crohn’s disease is effective despite previous pharmacodynamic failure

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Introduction: The outcome of crohn’s disease (CD) patients who failed anti-TNFα therapy despite adequate serum drug levels (pharmacodynamic failure) is unclear. Aims: We aimed to assess such pediatric patients who underwent intestinal resection and were re-treated with the same anti-TNFα agent post-operatively.

Methods and Materials: Pediatric CD patients who underwent intestinal resection and were treated with anti-TNFα agents post-operatively were assessed retrospectively. Patients were stratified to those with pre-operative anti-TNFα pharmacodynamic failure and those with no pre-operative anti-TNFα treatment.

Results: A total of 61 children were included, 21 with pharmacodynamic failure and 40 controls. Median age at intestinal resection was 15 years with 28 (46%) females. The median time from intestinal resection to anti-TNFα initiation was 7 months (IQR 4-13 months). At the time of post-operative anti-TNFα initiation there were no differences in clinical, laboratory and anthropometric measures between groups. Similar proportions of patients from both groups were in clinical remission on anti-TNFα treatment after 12 months and at the end of follow-up (1.7 years, IQR 1-2.9 years): 90.5% vs. 87.5% and 85.7% vs. 82.5% for pharmacodynamic failure patients and controls, respectively; p=0.8. No significant differences were observed at 14 weeks and 12 months of post-operative anti-TNFα treatment including endoscopic remission rate and fecal calprotectin. Both groups significantly improved all measures during post-operative anti-TNFα treatment.

Conclusions: Pediatric CD patients who failed anti-TNFα therapy despite adequate drug levels and underwent intestinal resection can be re-treated with the same agent for post-operative recurrence with high success rate similar to anti-TNFα naive patients.

P073. Infliximab induced psoriasis in a cohort of children with inflammatory bowel disease : a 12 years follow-up study.

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Objectives and study: In adult inflammatory bowel disease (IBD), skin adverse reactions have an estimated prevalence of 1.6 to 22%. This side effect occurs more frequently in patients treated with infliximab (IFX) for IBD. Data in the pediatric population are lacking so far.
Methods: All patients aged 2 to 18 years, with Crohn’s disease (CD) or Ulcerative colitis (UC) and treated for the first time by IFX between January 2002 and March 2014, were considered for inclusion in this monocentric retrospective study.

Results: 20 patients (14% of the cohort) had an IFX-induced psoriasis. 70% of them (n = 14) were in remission when the psoriasis was diagnosed. Psoriasis was diagnosed at the 8th injection (6; 15), though 355 (239; 532) days after the start of biotherapy. 20% of patients had a combo therapy: 50% of them were treated by 6-mercaptopurine, 25% by azathioprine and 25% by methotrexate. The median IFX trough levels (TRI) when psoriasis occurrred was 4.7 mcg / mL (1.8; 9.6) and 4.1 mcg / mL (2.1; 8.8) at the previous visit. Median Antibodies to IFX (ATI) rate was 0%. All were supported by local treatments. No patients discontinued biotherapy following the psoriasis. Personal or family history of psoriasis, and the smoking status have not been collected. We compared the population of patients with psoriasis (n = 20) and without psoriasis (n = 127) with an univariate model. All children in the psoriasis group were followed for a CD. There was more perineal location of CD in psoriasis group with a significant difference (p = 0.033).

Conclusion: 14% of our IBD patients treated with IFX developed psoriasis during follow-up. All were CD, more frequently it occurred for CD with perineal lesions, at the 8th injection in median, with no ATI.

P074. Skin manifestations in monoclonal therapy of Pediatric inflammatory bowel disease (PIBD).

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Background: Skin lesions in PIBD can occur as extraintestinal manifestations of IBD, with an averagely reported incidence of 15%. However, skin lesions triggered by monoclonal therapy in PIBD are little known and under-reported in literature.

Aim: To describe skin changes after commencement of monoclonals in PIBD patients.

Methods: Retrospective review of medical records from PIBD patients who developed skin lesions while on monoclonals and were further referred for dermatology opinion between 2013 and 2017. Minor local cutaneous manifestations at injection site were excluded.

Results: 22/752 (2.9%) PIBD patients were referred, 8/12 Crohn’s disease (59%), 5/12 UC (32%) and 1/12 IBD-U (8%). 11 patients were on Infliximab and 11 on Adalimumab. Females were twice frequently affected, age ranged from 6 to 17.7 years (mean of 8.4). 8/22 patients (36.6%) needed skin biopsies in order to clarify the diagnosis. Four groups were identified, group A: Patients with skin lesions highly likely to be secondary to monoclonal treatment 10/22 (45.5%); group B: patients whose lesions were secondary to the disease 5/22 (22.7%); group C: incidental findings 3/22 (13.6%) and group D: patients whose lesions were a combination of the above 4/22 (18.2%). For skin manifestations likely secondary to monoclonals, 4/10 followed Infliximab exposure and 6/12 followed Adalimumab. Median latency for lesions onset was 1.6 years (range 0.4-3.3). No cases of malignancy or cutaneous infections were reported. Monoclonal therapy was maintained in all cases. Clinical features of patients with monoclonal-induced lesions are summarised in table 1.

Conclusion: Skin lesions in PIBD patients receiving monoclonals were considered to be drug-induced in almost half of the cases. Psoriasis and psoriasiform lesions were commonly seen with Infliximab; however, no pattern could be identified for Adalimumab-induced skin lesions. Prompt referral for dermatology assessment in PIBD patients receiving monoclonals is advised.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age (years)</th>
<th>IBD subtype</th>
<th>Biologic</th>
<th>Latency (years)</th>
<th>Skin manifestation</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>13.7</td>
<td>CD</td>
<td>IFX</td>
<td>0.4</td>
<td>Psoriasis</td>
<td>Ears, knee, elbow</td>
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<tr>
<td>2</td>
<td>Male</td>
<td>15.8</td>
<td>IBDU</td>
<td>IFX</td>
<td>0.5</td>
<td>Psoriasis</td>
<td>Scalp, face, ears, hands, feet</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>11</td>
<td>CD</td>
<td>IFX</td>
<td>0.8</td>
<td>Psoriasis</td>
<td>Scalp, chin, ears, knees</td>
</tr>
<tr>
<td>4</td>
<td>Female</td>
<td>16</td>
<td>CD</td>
<td>IFX</td>
<td>1.3</td>
<td>Eczematous patches</td>
<td>Lateral abdominal, knuckles</td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>10.4</td>
<td>ADA</td>
<td>IFX</td>
<td>2.4</td>
<td>Psoriasis</td>
<td>Generalised including scalp</td>
</tr>
<tr>
<td>6</td>
<td>Male</td>
<td>13</td>
<td>UC</td>
<td>ADA</td>
<td>1.4</td>
<td>Psoriasis</td>
<td>Arms, legs</td>
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<td>7</td>
<td>Female</td>
<td>14.4</td>
<td>UC</td>
<td>ADA</td>
<td>1.6</td>
<td>Psoriasis</td>
<td>Lower legs bilaterally</td>
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<tr>
<td>8</td>
<td>Female</td>
<td>12.9</td>
<td>CD</td>
<td>ADA</td>
<td>2.3</td>
<td>Psoriasis</td>
<td>Scalp, eye brow</td>
</tr>
<tr>
<td>9</td>
<td>Female</td>
<td>9.8</td>
<td>CD</td>
<td>ADA</td>
<td>2.0</td>
<td>Psoriasis</td>
<td>Face</td>
</tr>
<tr>
<td>10</td>
<td>Female</td>
<td>6.3</td>
<td>UC</td>
<td>ADA</td>
<td>3.3</td>
<td>Psoriasis</td>
<td>Sheen and torso</td>
</tr>
</tbody>
</table>

P075. Shared decision making in the choice of anti-TNF alpha in Pediatric crohn's disease

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Introduction: Infliximab (IFX) and Adalimumab (ADA) are the two approved anti-TNFα drugs for Paediatric Crohn’s disease (P-CD) treatment. In our center, some families are invited to participate in the choice of the anti-TNF. Our aim is to analyze baseline characteristics and outcomes of this group of patients, comparing with the group who are not given the option of shared decision.

Methods: retrospective study of P-CD patients (<18 years) who initiate anti-TNFα therapy between July 2007 and December 2015. T-student test was used for quantitative variables and Chi-square for qualitative ones.

Results: Sixty-six patients were included; 56% (n=37) were given the option to choose the drug and 44% (n=29) were not. There were not statistically significant differences between sex, age and disease duration between both groups. The reasons for not offering a shared decision making were: 20 with specific clinical presentation, 3 social reasons, 1 treatment started in other center and 5 cause not known. In the group that elected the treatment 89% (n=33) chose ADA versus 11% (n=4) that preferred IFX, while in the other group 72.4% (n= 21) start IFX and 27.6% (n=8) initiated ADA, showing significant statistically differences (p<0.05). Regarding PCDAI at the start of anti TNFα, a lower mean value (19.59) was observed in the choice versus non-choice group (33.69) (p <0.05). Regarding remission...
rate (6 and 12 months) after starting biologic treatment no statistically significant differences were found between those who chose (100% and 95.2%) and those who did not (84.6% and 89.5%), nor among those who chose ADA or IFX (p> 0.05).

Conclusions: The choice of the anti-TNF-α drug by a selected group of patients with P-CD doesn't influence the response and the course of the disease, being a safe practice. Most of our patients choose ADA, probably in relation to the administration route.

P076. Vedolizumab for steroid refractory Ulcerative Colitis unresponsive to anti-TNF; a single centre experience

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Vedolizumab is a humanised monoclonal antibody. The antibody targets α4β7 integrin which recruits white blood cells to inflamed gut tissue. Effective treatment reduces the white cell influx. Studies in adults have demonstrated the efficacy of this treatment however, paediatric data are scarce. We present our experience of Vedolizumab in children facing imminent colectomy with disease refractory to steroids and anti-TNF despite concomitant azathioprine. A retrospective review of prospectively collected data was performed in a UK centre which provides paediatric gastroenterology services for 10 hospitals and a population of 5.4 million. Children with IBD are diagnosed according to Porto criteria and managed following ESPGHAN guidelines. We have treated 4 boys with Vedolizumab for UC refractory to anti-TNF. The boys were aged 6, 8, 13, and 14 at diagnosis and started anti-TNF for disease refractory to steroid treatment while receiving azathioprine 16, 27, 2 and 13 months post-diagnosis. All had 5mg/kg of anti-TNF at 0.26 weeks. Two patients showed no response (ability to wean steroids). Two children showed partial response but this was not sustained despite 6 weekly and 4 weekly dosing respectively. All children had active colitis at endoscopy pre Vedolizumab and were offered the choice of colectomy or Vedolizumab. Anti-TNF was stopped and 300mg of Vedolizumab was given at 0,2,6 weeks and thereafter 8 weekly. PUCAI at first Vedolizumab infusion was 55, 60, 25 and 45 and was 5, 45, 25 and 14 at weeks. Two children stopped prednisolone and remain in remission on 8 weekly dosing and azathioprine after 10 and 4 months respectively. Two children required colectomy for refractory disease. These few cases demonstrate that Vedolizumab can be a colectomy sparing strategy for patients with refractory UC. Longer term outcome needs to be assessed.

P077. Therapeutic approaches for perianal fistula in Pediatric and adolescent onset Crohn’s disease-a multicentre cohort study

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Introduction: There is no consensus on the management of Crohn’s disease related perianal fistulae (CD-PAF) in paediatrics Aims: to evaluate therapeutic interventions and their efficacy in a multicentre (7) cohort with paediatric and adolescent onset CD-PAF.

Methods: Patients with paediatric/adolescent onset CD-PAF diagnosed since 2010 and having follow-up data of at least 6 months since diagnosis. Complete clinical fistula healing was defined as absence of any draining fistulas on clinical examination. Re-interventions were defined as need for: repeat abscess drainage, seton reinsertion, diverting stoma or proctectomy. Univariate and multivariate analysis was done for predictors of fistula healing and re-intervention.

Results: 116 patients were included (74 boys and 42 girls). The mean age at diagnosis of fistula was 12.9 years. MRI was done in 85 of the patients with complex fistula in 57 (67%). Proctitis at presentation in 33%. 55% had abscess drainage but only 17 had seton. After diagnosis there was significant increase in the use of biologics (13.7% before and 83% after) and immunosuppressant (29% before and 80% after). There was significant difference in healing based on type of fistula (simple fistula 78%, complex fistula 26%, p=0.001). Follow-up MRI scan (n=40) demonstrated 29 with partial and 6 with complete healing. Anti-TNFs were continued in 86 patients.10 patients stopped anti-TNFs (6-planned withdrawal, 4-patient preference), 7 had recurrence of perianal fistula. 16% of the patients required re-intervention (UA and abscess drainage, diverting stoma-3 and reinsertion of seton-2). Complex fistula type (p=0.015), those with proctitis (p=0.04) and those needing abscess drainage (p=0.02) were more likely to need re-intervention and patients with anti-TNF therapy (0.01) less likely to need repeat surgery.

Conclusion: Combined medical and surgical management is paramount. Significant proportion of patients had complete or partial clinical healing. Repeated surgical intervention in CD-PAF was only required in 16% of the patients.

P078. Differences in therapy approaches and outcomes in Pediatric and adult onset perianal fistulising Crohn's: comparing 2 ecco collaborative fistula cohorts

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Introduction: There is no comparative data on outcomes in perianal fistulas in paediatric/adolescent versus adult onset CD. Management paradigms in perianal fistulas in Crohn’s disease is not fully defined and approaches from paediatric and adult IBD clinicians and surgeons may be different.

Aims: We aimed to study any differences in diagnostic and treatment approaches and outcomes in paediatric/adolescent onset CD with perianal fistula (CD-PAF) and adult onset disease.

Materials and Method: Data was collected on patients included in 2 retrospective multicentre multinational cohorts (11 adult and 7 pediatric centres) of perianal fistula with paediatric/adolescent onset and adult onset CD PAF. We evaluated fistula characteristics, surgical and medical treatments following onset of CD-PAF and fistula healing. We also compared re-intervention rates: the need for re-insertion of seton or abscess drainage or diverting stoma or proctectomy.

Results: 253 adults and 116 paediatric/adolescent patients were included. Complex fistulas were identified in 53% of adult onset and 67% of paediatric/adolescent group. Proctitis was recorded in 43% of adult onset and in 3% of paediatric/adolescent onset CD-PAF. Significantly higher proportion of adult CD-PAF patients had seton insertion (15% vs 54%, p<0.001). Anti TNF use was more often in paediatric onset CD-PAF (83% vs 68%). Complete clinical fistula healing was more often noted in paediatric/adolescent onset CDPAF (71% vs 49%, p=0.015). Reintervention rates were higher in adult onset CD (40.3% vs 16.05%, p= <0.001. Radical surgery (diverting stoma or proctectomy) was required in 3 patients (2.58%) with paediatric/adolescent onset and 26 patients (10.28%) with adult onset CD-PAF (p=0.04).

Conclusion: Paediatric/adolescent onset CD-PAF appears to have better outcomes with less radical surgery or re-interventions when compared to adult onset disease despite less frequent use of seton.
This is a single centre retrospective study evaluating how high was in 2011-2016 operative ratio, how many surgeries were elective resp. Laparoscopic, which operation type was predominant, and how many acute reoperations were needed. From 2011 to 2016 we newly diagnosed using Porto criteria 99 patients with Crohn’s disease, 61 males (62%). Patients were aged from 1.5 to 18.5 years (average 13.05±3.88 y).

Results: In the same period 25 of 99 patients required surgery (25%), 14 boys (56%). Age of operated patients was from 6.3 to 18.5 years (average 15.51±2.48). Period from diagnosis to surgery was 0 to 60 months (average 12.08±17.4). 24/25 (96%) patients underwent IC resection, 1 had resection of jejunal stenosis. 18 interventions were elective (72%) and 7 acute (28%); in 4 patients the diagnosis was unknown prior to surgery, 3 had acute intestinal obstruction. 4 operated patients (18%) required acute reoperation, 3 because of postoperative ileus, 1 because of different cause. Laparotomic access was chosen if complications were expectable, i.e. 11 patients (44%) including those 7 acute ones, miniinvasively initiated 14 operations (56%), where the isolated stenosis was probable, but just 7 were miniinvasively completed (28%). All those completed laparoscopic operations were elective and we did not meet any acute postoperative complication. The conversion to laparotomy was due to complicated intraabdominal adhesions in all 7 cases, but without acute postoperative complications. The number of acute reoperations was higher in those non-elective operations (P<0.05).

Conclusion: There were 25 of 99 newly diagnosed patients with Crohn’s disease in years 2011-2016 who required operation: 7 acute (4 prior to diagnosis), 18 elective (72%), of those 7 completely miniinvasive (28%). There were 24 (96%) IC resections done and 1 stenosis of jejunum resected. Abdominal revision/reoperation were necessary only in acute laparotomic operations.

key words: Crohn’s disease, miniinvasive operation

P080. Postoperative midterm follow-up in patients with pediatric onset Crohn’s disease

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Background: Patients with Crohn's disease (CD) may require surgical treatment, depending on their medical condition or disease progression. However, limited data are available on the postoperative progression and prognosis of pediatric CD in Korea. This study was conducted to assess the preoperative and postoperative progression and prognosis of pediatric onset CD.

Methods: We reviewed medical records of patients diagnosed with pediatric CD who underwent surgery between February 2011 and April 2017 at Pusan National University Children’s Hospital. The surgery was divided into luminal surgery and perianal surgery. Patients who underwent surgery were examined for changes in ESR, height, weight, the duration of hospitalization and number of hospitalizations before surgery, and at 6 months, 1 year, and 2 years after surgery.

Results: A total of 158 patients were examined and 24 (15.2%) patients who underwent surgery were included. Of them, 12 patients (50%) underwent surgery for luminal CD, 9 (37.5%) for perianal CD, and 3 (12.5%) underwent both operations. In 15 patients who underwent luminal surgery, weight gain (P = 0.01) and change of ESR (P = 0.00) were statistically significant. However, increase in height was not statistically significant.

In comparison of the two groups according time showed no significance (P = 0.281). The average number of hospitalizations was decreased from 7.3 ± 11.4 times before surgery to 0.4 ± 0.4 times after surgery in all patients (P = 0.007). The annual hospital stay was also significantly reduced from 131.7 ± 165.2 days to 4.1 ± 7.0 days (P = 0.001).

Conclusion: This study showed that in operated with pediatric onset CD, weight increases, ESR significantly decreases, and the number of re-admissions and days of hospitalization tends to decrease significantly. Although medical treatment is very important for this disease, quality of life can be improved by timely surgical treatment.

P081. Clinical characteristics and surgical outcome of pediatric, adult, elderly patients with ulcerative colitis who underwent surgery in a single center

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Introduction: We perform surgery with same concept and surgical procedure for ulcerative colitis (UC) patients from infantile to advanced years in single center. Aims: The aim of this study is to evaluate the differences of clinical characteristics in surgical course between children and adults with UC. Material and Methods: Twenty hundred eighty three patients who underwent primary surgery for UC from 2001 to 2014 in our hospital were enrolled. Finally, all patients underwent total proctocolectomy and ileal pouch anal anastomosis (IPAA) by hand sewn procedure. Patients were divided into three groups by age at onset; pediatric onset (≤15 years of age, n=42), adult onset (≥16 years of age ≤49 , n=198), and elderly onset (≥50 years of age, n=43). Patients and disease characteristics, preoperative treatment, intestinal complication, operative procedure, and postoperative complication were evaluated among groups.

Results: Median age (years, range) at operation was 16.2 (2-40) in pediatric patients, 35.5 (17-69) in adult patients, and 63.2 (50-82) in elderly patients. Pediatric patients have more extensive colitis and a higher frequency of steroid dependency compared with adults and elderly patients. Disease severity in elderly patients was higher compared pediatric and adult patients. Preoperative disease duration in pediatric and elderly patients was shorter than adult patients. Three-staged operations were selected in 43% of elderly patients, 28% of pediatric patients and 15% of adult patients. Pediatric patients tended to have more frequency of postoperative complications such as surgical site infection, stoma outlet obstruction and pouchitis compared with adults and elderly patients.

Conclusions: Clinical characteristics of UC in pediatric and elderly patients who underwent surgery have a higher intractability compared with UC in adult patients.
P082. Fecal Microbiota Transplantation for Cytomegalovirus infection in pediatric patients with acute severe colitis

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Background: Acute severe colitis (ASC) is a very serious condition with high colectomy rate. Cytomegalovirus (CMV) infection may have deleterious effect on the clinical course of inflammatory bowel disease (IBD). Treatment of CMV infection in IBD includes ganciclovir with severe adverse events and discontinuation of immunosuppressive agents that could result in IBD flare. There are some reports on effectiveness of fecal microbiota transplantation (FMT) in CMV colitis, but FMT has never been studied as rescue therapy for ASC with CMV infection.

Methods: We report successfully treatment of CMV infection using FMT in patients with ASC. We used 10 FMT infusions, each 50 ml via nasogastric tube in each patient.

Results: Patient 1: A 4-years-old diagnosed with UC-2 years ago. He had been treated unsuccessfully with GCS, AZA, CsA and IFX. Six months ago he presented with ASC (PUCAI=85) and received GCS, metronidazole, cefotaxime (14 days) resulting in mild improvement (PUCAI=65). We found positive PCR DNA for CMV in colonic biopsies. We used FMT infusions, successfully (PUCAI=0), colonic CMV was negative. We put him on azathioprine. Half year later he is still in complete clinical remission.

Patient 2: A 10-years-old diagnosed with UC-6 years ago. He had been treated with GCS, AZA, calcineurin inhibitors, biologics (IFX, ADA). One year ago while on ASA, MTX he presented ASC (PUCAI=65) with GCS resistance. CMV PCR DNA in colonic biopsies was positive. We withdraw MTX and GCS and put him on FMT, with prompt clinical response (PUCAI=15). Colonic CMV was also negative. Six months later he was still in clinical remission.

Conclusion: We reported the first two cases of ASC with colonic CMV successfully treated with FMT. FMT may be a potential treatment option of ASC with CMV. However further studies are needed.

P083. Use of ferric carboxymaltose for the treatment of iron deficiency anaemia in children affected by inflammatory bowel disease

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INTRODUCTION Iron deficiency anaemia (IDA) is the most common systemic complication of paediatric inflammatory bowel disease (PIBD) with reduced quality of life, increased hospitalization and healthcare costs. Oral iron is usually ineffective and not well tolerated. Intravenous ferric carboxymaltose (FC) has been shown to be an effective and safe treatment of IDA in IBD adult patients but very few studies exist in its use in PIBD and almost none in children under 6 years.

AIM: To study the effectiveness and safety of FC in the treatment of IDA in PIBD

METHODS: We retrospectively reviewed all our PIBD patients with IDA treated with FC in the past 3 years. IDA was diagnosed by combining haemoglobin (HB), haematocrit (HCT), mean cell volume (MCV) and iron levels. Patients had a 15 minutes infusion of either 500 mg, 1000 mg or 1500 mg of FC according to body weight and HB levels. Bloods were repeated 4-6 weeks after each infusion.

RESULTS: Over the past 3 years we treated 56 PIBD patients with IDA, 29 females, 24 males; Crohn's disease =31, ulcerative colitis =13, IBD unclassified =9; median age 12 years (range 3-17); 7/56 were under 6 years (range 3-6); HB (g/L): pre median 104 (58-135), post median 124 (88-140); HCT (L/L): pre median 0.32 (0.22-0.40), post median 0.36 (0.27-0.42); MCV (fL): pre median 73.3 (57.5-86.8), post median 78.3 (62.2-90), iron level (mcg/L): pre median 6.7 (2.8-20.7), post median 13.4 (4.9-33.6). Only one patient developed an allergic reaction with shivering and fever 10 minutes into the infusion. In the 7/56 patients below 6 years of age we had the same efficacy and no adverse events.

CONCLUSIONS Our study shows that FC is safe and efficacious in the treatment of IDA in PIBD also in the younger children

KeyWords: anaemia, ferric carboxymaltose, paediatric inflammatory bowel disease

P084. Monitoring mucosal healing with faecal calprotectin in children with ulcerative colitis.

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Introduction: FC is a good marker in monitoring mucosal healing in adults. Its concentrations is related to state of mucosa.

Aim: To assess the usefulness of FC as a biomarker of mucosal healing in children with UC.

Material and methods: 81 patients with UC were involved to the study and had colonoscopy performed, FC and ESR measured, BMI and PUCAI calculated. We have identified two subgroups: patients with full mucosal healing (Baron score=0), and with inflammation. The ROC was used as a method to establish cut-off points. The cut-off points are FC threshold for simple model and posterior probability threshold for the LDA. The AUC assesses the differentialiation quality of the group based on the model score. To increase sensitivity at high specificity the LDA with FC, ESR, BMI and PUCAI was taken.

Results: AUC for the simple model was 0.86. The cut-off level of discrimination between subgroup with mucosal healing vs subgroup with inflammation was 274 μg/g with sensitivity 0.97 and specificity 0.62. When specificity was outweighed over sensitivity the cut-off point was 37 μg/g with sensitivity 0.32 and specificity 0.94. Due to the low sensitivity accompanying high specificity we used LDA with other parameters to increase sensitivity rate. With LDA used on FC, ESR, BMI and PUCAI the AUC was 0.88, and we could discriminate our patient with sensitivity 0.53 and specificity 0.96.
Conclusions: FC is a good marker of mucosal healing in children with UC. FC above 274 μg/g enable to select 62% of patients with inflammation in mucosa. LDA with FC, ESR, BMI and PUCAI let us select 53% of patients with full mucosal healing. Using these two methods, step by step, we could discriminate patients with unknown mucosa status, that requires endoscopy.

Keywords: children, faecal calprotectin, ulcerative colitis


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Introduction: FC is a good marker in monitoring mucosal healing in adults with CD. Its concentrations is related to state of mucosa observed in endoscopy.

Aim: To assess the usefulness of FC in predicting mucosal state in children with CD.

Material and methods: 68 patients with CD were involved to the study and had colonoscopy performed, FC level, CRP, HT measured and PCDAI calculated. Full mucosal healing was defined as SES-CD=0. We have identified two subgroups: patients with full mucosal healing, and with inflammation . The ROC was used as a statistical method to establish cut-off points. The cut-off points are FC level for simple model and probability threshold for the logistic regression. The AUC assesses the differentiation quality of the study group based on the model score. To increase specificity at high sensitivity the logistic regression with other predictors was made. The final model was selected using cross-validation.

Results: AUC for the simple model was 0.86. The selected cut-off level of discrimination between subgroup with full mucosal healing vs. subgroup with mucosal inflammation was 59 μg/g with specificity 0.94 and sensitivity 0.56. When sensitivity was outweighed over specificity the cut-off point was 1442 μg/g with specificity 0.36 and sensitivity 0.94. With logistic regression on FC, CRP, HT and PCDAI the AUC was 0.85, and we could discriminate our patient with specificity 0.50 and sensitivity 0.94.

Conclusion: FC is a good marker of mucosal healing in monitoring of children with CD. FC below 59 μg/g enable us to select 56% of patients with full mucosal healing. Logistic regression with FC, CRP, HT and PCDAI let us select 50% of patients with inflamed mucosa. Using these two methods, step by step, we could discriminate 44% of patients with unknown mucosa status, that require endoscopy.

Keywords: children, Crohn's disease, faecal calprotectin,


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Introduction: FC is a good marker in monitoring mucosal state in children with IBD. Due to increasing need in rapid, cheap testing for FC, especially in children, new point-of-care tests (POCT) are being developed.

Aim: Comparison of rapid immunochromatographic test (POCT) with standard enzyme-linked immunoassay (ELISA).

Material and methods: 20 children with IBD were involved in the study and had colonoscopy performed. Each patient had CRP, ESR and FC measured by two assays (ELISA and POCT). Full mucosal healing was defined as Baron score or SES-CD of 0. Results of FC were correlated with each other, with endoscopic findings, CRP and ESR by Spearman's rank correlation coefficient. We have identified two subgroups: patients with full mucosal healing, and with inflammation lesions. The ROC was used as a method to establish cut-off points. The AUC assesses the differentiation quality of the study groups. The Deming regression was used to determine systematic differences between two measurement methods.

Results: Although both FC methods correlated significantly with r=0.63, slope and intercept differed extensively, with up to 3-fold quantitative differences between assays (y=2.8x-432). The AUC for the ELISA and POCT was 0.89 and 0.82 respectively. The selected cut-off level of discrimination between subgroup with full mucosal healing vs subgroup with mucosal inflammation present was 686 μg/g with sensitivity 0.75 and specificity 0.88 for ELISA and 260 μg/g with sensitivity 0.83 and specificity 0.88 for POCT. The ELISA had stronger, clinically significant correlation with presence of inflamed mucosa then POCT with r=0.66 and r=0.55 respectively and with CRP r=0.39 and r=0.29, but not with ESR r=0.31 and r=0.52.

Conclusion: POCT and ELISA showed comparable clinical performance in finding inflammation lesions. However the cut of points for detection of inflammation differed extensively between methods.

Keywords: children, faecal calprotectin, inflammatory bowel disease

P087. Home or hospital-based analysis of stool calprotectin: assessing two methods for monitoring inflammatory bowel disease

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Background and aims: Repeated stool calprotectin measurements are increasingly used to monitor asymptomatic patients with inflammatory bowel diseases. Recently a lateral flow-based rapid test was launched that allows patients to measure stool calprotectin values at home. It comes together with a software application (IBDoc®) that turns a smartphone camera into a reader. We compared this new, by patients, performed method with the hospital-based lateral flow reader Quantum Blue®(QB) and the enzyme-linked immuno sorbent assay (ELISA) to see whether these tests agreed sufficiently.

Methods: In a single center method comparison study, we asked 101 teenagers and adults to perform the IBDoc® measurement at home. Next the residual of the extraction fluid and a fresh specimen from the same bowel movement were sent to our hospital where they were tested with the QB reader and ELISA respectively.
P088. Role of fecal calprotectin as predictor of endoscopic activity in pediatric patients with ulcerative colitis

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Introduction: Colonoscopy is the “gold standard” in the IBD diagnosis. However it is not suitable for regular disease monitoring especially in children. Fecal calprotectin (FC) is a reliable noninvasive marker of intestinal inflammation. It appears that measuring FC can detect subclinical inflammation and thus identify patients at high risk for disease relapse.

Aims: The aim of this study was to assess the role of FC as predictor of endoscopic disease activity in pediatric patients with ulcerative colitis (UC) in clinical remission.

Material and methods: 24 children – 14 girls and 10 boys took part in the study (median age 15 years, range 2-17 years). A total of 34 visits were included. Clinical remission was defined as Pediatric Ulcerative Colitis Activity Index <10. All participants underwent a routine follow-up colonoscopy. Endoscopic findings were assessed according to the Mayo endoscopic subscore. Mayo ≤ 1 was accepted for endoscopic remission. Additionally all participants provided fresh fecal samples for measurement of FC. FC levels were determined by a rapid quantitative test based on lateral flow immunochromatography (Quantum Blue® Calprotectin High Range, Bühlmann Laboratories AG).

Results: There was a strong positive correlation between the FC levels and the endoscopic disease activity (n=34; r=0.83, p<0.001). The median FC levels in the subgroup with endoscopic activity (Mayo ≥3) were significantly higher than the median FC levels in the subgroup without endoscopic activity (Mayo ≤1) (1000 µg/g, IQR 575-1800 µg/g vs. 100 µg/g; IQR 60-223 µg/g; p<0.001). At a cut-off 298.5 µg/g FC had 92.3% sensitivity, 95.2% specificity and an AUROC 0.974 (SE 0.023; 95% CI 0.930-1; p<0.001) to predict endoscopic activity.

Conclusions: FC is an accurate surrogate marker of endoscopic activity in children with clinically quiescent UC.

Keywords: fecal calprotectin, pediatric ulcerative colitis, endoscopic activity

P089. role of fecal calprotectin as predictor of endoscopic activity in pediatric patients with Crohn’s disease

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University Pediatric Hospital, Sofia, Bulgaria

Introduction: Colonoscopy is the “gold standard” in the IBD diagnosis. However it is not suitable for regular disease monitoring especially in children. Fecal calprotectin (FC) is a reliable noninvasive marker of intestinal inflammation. It appears that measuring FC can detect subclinical inflammation and thus identify patients at high risk for disease relapse.

Aims: The aim of this study was to assess the role of FC as predictor of endoscopic disease activity in pediatric patients with Crohn’s disease (CD) in clinical remission.

Material and methods: 18 children – 10 girls and 8 boys took part in the study (median age 15 years, range 9-17 years). A total of 34 visits were included. Clinical remission was defined as Pediatric Crohn’s Disease Activity Index <10. All participants underwent a routine follow-up colonoscopy. Endoscopic findings were assessed according to the Simple endoscopic score for Crohn’s disease (SES CD). SES-CD ≤ 1 was accepted for endoscopic remission. Additionally all participants provided fresh fecal samples for measurement of FC. FC levels were determined by a rapid quantitative test based on lateral flow immunochromatography (Quantum Blue® Calprotectin/ Quantum Blue® Calprotectin High Range, Bühlmann Laboratories AG).

Results: There was a strong positive correlation between the FC levels and the endoscopic disease activity (n=34; r=0.87, p<0.001). The median FC levels in the subgroup with endoscopic activity (Mayo 2-3) were significantly higher than the median FC levels in the subgroup without endoscopic activity (Mayo ≤1) (1000 µg/g, IQR 575-1531.75 µg/g vs. 97 µg/g; IQR 30-127 µg/g; p<0.001). At a cut-off 298.5 µg/g FC had 93.75% sensitivity, 86.67% specificity and an AUROC 0.973 (SE 0.023; 95% CI 0.927-1; p<0.001) to predict endoscopic activity.

Conclusions: FC is an accurate surrogate marker of endoscopic activity in children with clinically quiescent CD.

Keywords: fecal calprotectin, pediatric Crohn’s disease, endoscopic activity

P090. Quality of life in Pediatric Crohn’s disease: data from the imagekids study

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BACKGROUND: The evaluation of health-related quality of life (HRQOL), using the validated disease-specific IMPACT-III questionnaire, has a key role in ascertaining the effect of disease on patients with Crohn’s disease (CD). We sought to describe HRQOL variations across a large prospective cohort of pediatric CD patients.

METHODS: We used the prospectively collected data from the ImageKids study (a multicenter, multinational study designed to develop the pMEDIC and PICMI scores for magnetic resonance enterography) on children diagnosed with CD. IMPACT-III (35-item self-administered scale) was used to assess HRQOL in this cohort.

RESULTS: Data from 180 patients were analyzed, 94 males (52.2%) with a mean age of 14.2±2.2y and a median of 27 month (IQR 0.05-4.2) of follow-up. According to wPCDAI, 29.0% of patients were in clinical remission, whereas 39%, 13%, and 19% had mild, moderate, and severe disease, respectively. IMPACT-III total score had a poor but significant correlation with degree of mucosal inflammation judged by the SES-CD (r = -0.285, p < 0.0001). Correlation was strong with clinical activity judged by wPCDAI (r = -0.550, p < 0.0001). Patients with higher disease activity had lower total IMPACT-III score, as did the 4 domains (wellbeing, emotional functioning, social functioning, and body image, Table I). Differences across wPCDAI groups were higher for wellbeing and lower for body-image domains. Patients with perianal disease had lower wellbeing (p = 0.026) and body image (p =0.004) domain scores. Steroid treatment was associated more with lower emotional functioning score than enteral nutrition was (p = 0.028).

CONCLUSIONS: In this ImageKids cohort, HRQOL was lower in patients with higher disease activity and in those with perianal disease. An awareness of which domains within IMPACT may be differentially affected by various therapies or disease characteristics could help the clinician by focusing interventions (ie, psychological) to address these areas of concern.

QOL-imagekids-table-1.pptx (could not be inserted)

P091. Quality of life in pediatric IBD. What is the parental and peers perspective?

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Introduction - About 25% of inflammatory bowel disease (IBD) diagnosis are established in paediatric age. IBD deeply affects physical and psychosocial functioning of children/adolescents, generating changes in the quality of life (QoL) perceived by the elements of their social environment, especially their parents. Only recently, rare paediatric studies have addressed QoL issues both in the parental and peers’ perspective.

Aims - Our primary aims were: to evaluate the correlation between QoL assessed by: a) pediatric IBD patients and their parents; b) pediatric IBD patients and their healthy peers.

Material and methods - Clinical and sociodemographic data were collected and the IMPACT-III and PedsQL TM 4.0 questionnaires were applied to 13 paediatric IBD patients, mean age 15.5 years (9-18 years). The same questionnaires were applied to their caregivers, predominantly mothers. Additionally, the PedsQL TM 4.0 was applied to 35 healthy adolescents, mean age 15.6 years (14-18 years). Descriptive and inferential analysis were performed.

Results - High levels of agreement between QoL reported by the patients and parents were found in both questionnaires (ICC 0.83-0.88), although, parents tended to underestimate their children QoL (not statistically significant). When compared with healthy peers, the IBD group presented significantly lower QoL (p<0.003), particularly in the physical (p=0.0001) and school functioning (p=0.003) domains. The two questionnaires revealed a good correlation in the patient group, which was less obvious in the parental group. Clinical and sociodemographic data were not significantly correlated to QoL scores.

Conclusions – Concerning our preliminary data and accordingly to previous studies, the parents of IBD paediatric patients may act as suitable proxies for their QoL; as expected, QoL of IBD patients is lower than that of healthy peers, irrespectively of clinical scores. The potential usefulness of these instruments in this setting deserves further evaluation.

Key-words: Inflammatory Bowel Disease; Paediatric; Quality of Life; Parent-proxy

P092. Quality of life in Pediatric Inflammatory Bowel Disease Patient: Correlation with Clinical Characteristics.

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Introduction and aims: Inflammatory bowel disease (IBD) is a chronic relapsing disease which can negatively affect the quality of life (QoL) of the patient. IMPACT-III is the most commonly used validated questionnaire developed for determining the QoL of pediatric IBD patients.

In this study, we searched out current status of the QoL in Korean pediatric IBD population in accordance with their clinical parameters to investigate the relationships between them.

Material and Methods : Sixty-two children and adolescent IBD patients followed at Severance Children’s Hospital were enrolled to the study. Questionnaire including IMPACT-III were carried out. Basic demographics, clinical data such as disease phenotype, disease activity score, past history and current medications were collected from the medical records. Clinical factors affecting QoL were investigated.

Results: High Pediatric Crohn’s disease activity index (PCDAI) was significantly associated with poor IMPACT-III score (R=-0.428, p=0.004). However, Pediatric Ulcerative colitis activity index (PUCAI) did not correlate significantly with IMPACT-III score (R=-0.040, p=0.874). CD and UC did not show significant total IMPACT-III score differences (137.5(130.0-148.0) vs. 140.5(126.0-147.0), p=0.828). Disease phenotype according to Paris classification, past surgery history and current medications did not affect total IMPACT-III score significantly. According to the questionnaire, the most irritating problems that patients underwent were hospital visit and medical examinations (34%), food restriction (24%), IBD related symptoms (23%). About 69% of the patients felt that the disease did not affect their school performances whereas the disease negatively affected to their school performance in 21% of them, and positively affected in 10% of them.

Conclusion : As IBD is a lifelong disease, concerning about the health related quality of life is significant part of the management, especially for children and adolescents. Clinicians should consistently consider the QoL of the patients and try to improve it by ameliorating modifiable factors.
Background/Objectives: Young patients with inflammatory bowel disease (IBD) are at risk for developing anxiety and depression. This often negatively impacts disease activity and quality of life. Previous studies report conflicting prevalence, ranging from 10-45%. This study aims to describe the prevalence of anxiety and depressive symptoms in a Dutch cohort of young IBD patients, and to identify demographic and clinical predictors.

Methods: This study shows baseline data of a larger trial. IBD patients (N=374; 10-25 years) were screened for anxiety/depression and quality of life (QoL) using age-specific questionnaires (Screen for Child Anxiety Related Disorders (SCARED;10-20 years); Hospital Anxiety and Depression Scale (HADS-A; 21-25 years); Child Depression Inventory (CDI; 10-17 years); Beck Depression Inventory (BDI-II; 18-25 years); Impact-Ill, IBD-Q). Patients with elevated scores for anxiety/depression received a psychiatric interview assessing severity, leading to 3 subgroups: patients with no (“A”), mild (“B”) or severe (“C”) symptoms. Demographic and clinical characteristics were retrieved from medical charts. Group differences were assessed by One-way ANOVA, Kruskal Wallis and Chi-Square-analysis. Multivariate analysis identifying predictors of anxiety/depression will be performed.

Results: Most patients (mean age 18.9 (SD 4.1), 44.1% male) had Crohn’s disease (60.4%). Disease activity was mild, moderate and severe in respectively 19.5%, 2.7% and 2.1%. The majority (76%) was in clinical remission. 52.4% had no psychological symptoms, 35.2% mild and 12.4% severe. Elevated symptoms of anxiety (SCARED ≥30, ≥26, HADS-A≥8), depression (CDI≥13, BDI≥14) and both were found in respectively 28.6%, 3.0% and 15.9%. Group C had more severe disease than A (p<0.001) and B (p<0.001). Group A had longer disease duration and higher QoL than Group B (p=0.007; p<0.001) and C (p=0.015; p<0.001).

Conclusions: Considering the high prevalence of anxiety and depression, screening is recommended in young IBD patients. Identification of clinical risk factors guides clinicians to recognize vulnerable patients.

Keywords: Anxiety, Depression, Inflammatory Bowel Disease, Adolescents

Background/Objectives: Transition from pediatric to adult medical care in inflammatory bowel disease (IBD) patients should be a continuous, individualized and planned process. Our aim was to assess the satisfaction degree of IBD patients on our new transition program after the program.

Methods: Our transition program developed since 2008, includes a joint meeting with schedule planning and post-planned process. Our aim was to assess the satisfaction degree of IBD patients on our new transition program and post-program.

Results: From 2004 to 2016, 32 patients, 16 boys (50%), 22 (73%) were included in new program, 18 (56%) ulcerative colitis, 12 (38%) Crohn’s disease and 2 (6%) undetermined colitis. The median follow-up from diagnosis was 6 years (range 1.5-14 years). Only 4 (12.5%) patients moved in the active phase of the disease. 27 (84%) patients reported having received enough information prior to transition; 25 (78%) felt adequately prepared, 14 (44%) reported reluctance (6 lack of confidence, 8 fear of overcrowding). 94% of the patients included in the new program expressed a “good”/“very good” satisfaction degree. Both patients with no (“A”), mild (“B”) or severe (“C”) symptoms.

Materials and Methods: 30 children with IBD, mean age 13.1 years, treated with infliximab participated. Anemia was defined by WHO criteria. Remission was defined as PCDAI or PUCAI ≤10, normal CRP and albumin. HRQL was assessed with the PedsQL 4.0 Survey. Published data were extracted from Kunz, JH et. al, Inflamm
Bowel Dis. 2010;16:939 and Varni, JW et al. Medical Care 2001; 39: 800. Mean scores and proportions of patients with low scores predicting poor HRQL (“risk scores”) were compared with two-sample t test and Fisher’s exact test respectively; p<0.05 defined statistical significance.

Results: Comparisons within our cohort revealed lower mean scores and higher proportion of subjects with risk scores in active vs. quiescent disease, in patients with anemia vs. normal Hb in the entire cohort and in patients in remission but not in those with active disease. Compared to published IBD mean scores were lower in our entire cohort, in patients with anemia and in patients with quiescent disease plus anemia. In contrast, patients in remission with normal Hb scored higher. Compared to healthy controls mean scores were lower in all subgroups of our cohort except for patients with normal Hb and patients with quiescent disease plus normal Hb. Most statistically significant differences occurred in parent-reported scales.

Conclusions: Both disease activity and anemia impair HRQL in children with IBD. Our most intriguing finding was the deterioration of HRQL in anemic patients despite quiescent disease. We propose to include anemia-free remission into the list of quality of care indicators in pediatric IBD.

P096. Oral implementation of EEN is a good tolerated method to induce remission and normalize nutritional status in children with active CD.

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Background: The aim of treatment with EEN in children with active CD is both to reduce inflammation and to optimize nutritional status.

Methods: 20 children with active CD were treated for 6 weeks by EEN with Modulen IBD. Disease activity, intensity of inflammation and nutritional status were assessed at baseline and at 4 week after the end of treatment. At the final point the tolerance of nutrition therapy was evaluated as well. The statistical significance for PCDAI and calprotectin concentration was measured by the Wilcoxon signed-rank test.

Results: The mean reduction of PCDAI was statistically significant (from 26.3 ± 13.2 with the range of 57.5-10 to 7.8 ± 11.6 with the range of 52.5-0, p<0.05). Full remission (reflected by PCDAI<10) was achieved in 65%, clinical response in 30% and no response in 5% of children. The anti-inflammatory effect of therapy was stated based on the mean reduction of fecal calprotectin concentration (from 3380 mg/kg ± 7746 with the range of >30000-28 to 1046,6 mg/kg ± 1219 with the range of 4006-25, p<0,05). The flavour acceptance of Modulen IBD was observed - in the 95% of patients the oral intake of industrial formula was successfully realized during the whole duration of therapy. At baseline the 30% of children was undernourished (BMI below 3 percentile on WHO charts). In all patients the improvement of BMI status was stated. The mean increase of BMI was 0,91 kg/m²±0.4 and it was greater in the undernourished group (1.19 kg/m2 vs 0.62 kg/m2).

Conclusion: The six-week course of EEN is an effective method of treatment in children with active CD, that induces remission, reduces inflammation and normalizes the nutritional status. The observation of good oral tolerance of the nutritional plan, without the necessity of naso-gastric tube insertion, is the additional benefit with particular importance in pediatrics.

P097. Psychological and nutritional group intervention program in inflammatory bowel disease adolescent patients

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Background and objectives: Treatment adherence and healthy lifestyle in the adolescent patient with chronic diseases are challenging. The use of psychological and behavioral therapies are highly recommended to reduce anxiety and depression improving these issues. Educational group therapies are also useful to share fears and feelings with peers allowing to make behavioral changes to cope with the disease. Our aim is to evaluate the efficacy of a psychological and nutritional group intervention program in IBD adolescent patients.

Methods: Prospective pilot study evaluating a multidisciplinary program created ad hoc. The program involves 2 pediatric psychologists and a pediatric dietitian specialized in PIBD. The program includes 6 weekly sessions: 4 of them focused on emotional issues, and the other 2 (involving patients and their parents) on nutritional aspects. Evaluation of nutritional status including anthropometry, blood test and dietetic registration was performed at the beginning of the program. State-Trait Anxiety Questionnaire (STAI) and EnKid Questionnaire were performed at the beginning and at the end of the program.

Results: Eight PIBD adolescent patient (aged 13-17 years old) were included (6 girls; 6 Crohn’s disease, 2 Ulcerative Colitis). All patients completed the full program. At the end of the program, anxiety levels were reduced 50% according to the STAI questionnaire and adherence to Mediterranean diet increased from 30 to 60% according to EnKid Questionnaire. All participants evaluated the program positively and considered very beneficial the contact with PIBD peers.

Conclusion: A program focused on psychological and nutritional aspects is a useful intervention to reduce anxiety and to increase healthy nutritional habits in short-term follow-up. The program allows the adolescent patient to reach some coping strategies improving self-management on emotional and nutritional aspects. Medium and long term assessment is necessary to know the real impact of the program in their life.

Keywords: PIBD, adolescent, group therapies.

P098. Subjective versus objective assessment of nutritional status in Pediatric IBD (PIBD) in a tertiary center.

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Background and objectives: Improved care now (ICN) is a quality improvement collaboration of 96 PIBD centres with over 27,000 PIBD patients, helping clinicians to improve patient outcomes. One of the important PIBD outcomes is appropriate growth and nutrition. We used the ICN database to analyse the reliability of growth and nutritional data in our population.
hypoalbuminemia. The proportion of hypozincemia (defined as serum zinc level < 80 µg/dL) and serum zinc level were compared between IBD and non-IBD groups by using chi-squared test and t-test, respectively. Logistic regression analysis was performed to examine the association between hypozincemia and patients’ physical and disease condition. Factors affecting serum zinc level were analyzed using multiple regression model. P-value of less than 0.05 was considered to be significant.

Results: There was significantly more hypozincemia in children with IBD than the non-IBD group (71.9% vs. 55.2%, P<0.04). Serum zinc level was significantly lower in children with IBD than the non-IBD group (71±16µg/dL vs. 81±32µg/dL, p=0.01). Logistic regression analysis showed that sex (female) was significantly associated with hypozincemia. Serum albumin level was significantly associated with serum zinc level in addition to sex.

Conclusions: Our result suggests that hypozincemia was relatively common in children with IBD, and female and hypoalbuminemia were at risk of nutritional failure only and four (3Female) were at risk of growth failure only. BMI Z score identified only 3/14 patients with a Z score of > -2SD (2Female). Scores of -1 to -2 SD were 5(3Male) and scores of < -1SD were 6 (3Female).

Conclusions: Our incidence of growth and nutritional failure is in line with the ICN population average. However there was a discrepancy between SGA reporting and the actual BMI scoring, suggesting that SGA should be used along with other objective indicators in order to assess nutritional status in this population.

P100. Hypozincemia in children with IBD - a single center retrospective study

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Background and objectives: Zinc deficiency in children, caused by hypozincemia, may result in various symptoms such as eczema, diarrhea, impaired immune function, anorexia, and growth retardation. Children with inflammatory bowel disease (IBD) are considered as high risk group for hypozincemia because of inadequate intake, reduced absorption, or excess zinc consumption by inflammation. However there have been few reports about the hypozincemia and zinc deficiency in this population. The aim of this study is to examine proportion and related factors of hypozincemia in children with IBD.

Methods: In a retrospective review, pediatric patients aged 0-18yr whose serum zinc level was measured between 2012 and 2016 at gastroenterology division, National Center for Child Health and Development in Japan were recruited. The patients were classified into IBD group (64) and non-IBD group (87). The proportion of hypozincemia (defined as serum zinc level < 80 µg/dL) and serum zinc level were compared between IBD and non-IBD groups by using chi-squared test and t-test, respectively. Logistic regression analysis was performed to examine the association between hypozincemia and patients’ physical and disease condition. Factors affecting serum zinc level were analyzed using multiple regression model. P-value of less than 0.05 was considered to be significant.

Results: There was significantly more hypozincemia in children with IBD than the non-IBD group (71.9% vs. 55.2%, P<0.04). Serum zinc level was significantly lower in children with IBD than the non-IBD group (71±16µg/dL vs. 81±32µg/dL, p=0.01). Logistic regression analysis showed that sex (female) was significantly associated with hypozincemia. Serum albumin level was significantly associated with serum zinc level in addition to sex.

Conclusions: Our result suggests that hypozincemia was relatively common in children with IBD, and female and hypoalbuminemia were thought to be associated with hypozincemia in IBD patients. These results should be interpreted carefully having selection bias.

Keywords: IBD, hypozincemia, children

P101. Giant postinflammatory pseudopolypsis as a result of “healing” of ulcerative colitis in a 13-year-old girl

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Background and objectives: Postinflammatory pseudopolyps (PIPs) develop in connection with inflammatory process in the bowel. PIPs larger than 15 mm are classified as giant postinflammatory polyps. They are very rare, especially in children. This report presents a case of giant postinflammatory polyposis in young girl with history of ulcerative colitis.

Methods and results: We report a case of 13th year old girl, which suffered from ulcerative colitis and colonoscopic examination after achieving remission revealed multiple postinflammatory polyps – year 2013 (Fig.1). Histologic examination excluded adenomatous polyposis and dysplasia. We chose a conservative approach. After another year we performed surveillance endoscopy- year 2014 (Fig.2.). PIPs were smaller than in the previous endoscopic examination. Treatment of PIPs in
our patient is conservative yet. The fourth endoscopy was performed in year 2015. Endoscopic remission of UC continues. PIPs have been reduced (Fig 3.). Multiple biopsies with histological evaluation have found absence of active inflammation and dysplasia.

Conclusions: PIPs are non-neoplastic lesions resulting from regenerative process in the bowel. In our patient we repeatedly found giant PIPs in colon descendens and transversum. We suggest that it can be “hyperplastic” form of mucosal healing and maybe there exists some individual predisposition to this form of “healing”. Partial regression of giant polyps in our patient is demonstrated during the observation period. Surveillance colonoscopy is necessary also in the future.

Key word: childhood, intestinal polyps, ulcerative colitis

P102. Pulmonary necrobiotic nodules: a rare manifestation of Crohn's disease in pediatric patients

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Introduction: Pulmonary manifestations of Crohn’s disease are very unfrequent in paediatric patients. The findings of pulmonary nodules suppose an important challenge in diagnosis and treatment of these patients. We present the second reported case of necrobiotic pulmonary nodules in a paediatric patient and the first one treated with anti-TNF alpha on initial diagnosis.

Case description: A 14-year-old male, with no personal history of interest, who was admitted to hospital because of diarrhea, abdominal pain, anorexia and weight loss for three months. On physical examination the patient had affected appearance, pallor, supraumbilical pain and an anal fissure. The initial blood tests showed microcytic anemia, iron deficiency, hypoalbuminemia, thrombocytosis, elevated inflammatory markers (erythrocyte sedimentation rate, C-reactive protein and Fetal Calprotectin). Esophagogastroduodenoscopy, ileocolonoscopy and MRT enterography were compatible with colonic Crohn's disease. The patient started treatment with exclusive enteral nutrition, however it was discontinued after two weeks due to persistent digestive symptoms and poor adherence to treatment. In the examination prior to initiating anti-TNF alpha therapy (Infliximab), the chest X-Ray showed bilateral nodular lung lesions of peripheral distribution and the patient began to experience high fever, dyspnea, chest pain, musculoskeletal and dermatological manifestations. PET-CT showed hypermetabolic pulmonary nodular lesions, predominantly peripheral and a single cavity lesion. Autoimmune and infectious tests and tumor markers were negative. Lung biopsy was performed and the histological results reported necrobiotic abscessed nodules in relation to extraintestinal manifestation. Anti-TNF alpha treatment was initiated at standard doses aiming for improvement of digestive, musculoskeletal and dermatological symptoms in the first 24 hours and analytical, radiological and pulmonary function findings in 4 weeks.

Conclusion: Pulmonary necrobiotic nodules represent a rare extraintestinal manifestation of Crohn’s disease in pediatric patients (only one case has been reported in the literature). Anti-TNF alpha therapy can be an effective treatment, as occurs with another extraintestinal manifestations.

P103. Functional analysis implicating SAMD9 mutations in intestinal inflammation in patients with MIRAGE syndrome.

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Background and objectives: MIRAGE syndrome is caused by heterozygous mutations in the SAMD9 gene. The syndrome is characterized by enteropathy and is often fatal within first 2 years of life. However, pathogenesis of enteropathy in the syndrome is unknown.

Case and study methods: We present a case of MIRAGE syndrome (gestational age 35 weeks, birth weight 1330g) who developed restriction of growth, adrenal hypoplasia, genital anomaly, and enteropathy at the time of birth. Sigmodoscopy showed longitudinal ulcers in rectum. Apoptotic cells were observed at the mucosal biopsy specimen from the site of ulcer. To investigate the involvement of SAMD9 mutation in colitis, we transfected HEK293 cells with wild type (WT) or mutated (R1293W) SAMD9, and the difference in TNF-alpha responsiveness for apoptosis pathways were assessed using western blotting. (for what (PARP and XIAP) and why -pERK? – should probably mention the link between XIAP).

Results: R1293W transfected cells showed increased protein expression of cleaved Poly ADP-ribose polymerase (PARP) when compared with WT and control, which represented increased apoptosis in R1293W mutation. X-Linked inhibitor of apoptosis (XIAP) were decreased in R1293W mutations which may also explain the apoptosis observed in the patient intestinal mucosal biopsy.

Conclusion: Suppression of XIAP might contribute to increased apoptosis and intestinal inflammation observed in MIRAGE syndrome patients.

P104. A case of very Early Onset Inflammatory Bowel Disease initially presenting as Eosinophilic Colitis

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Objective: To illustrate the difficulty in diagnosing very Early Onset Inflammatory Bowel Disease (vEOIBD) in an infant who initially presented with bloody stools.

Case description/ Result: This is a case of a 8 months old Chinese girl who is the third child of a non-consangunineous marriage. She was born full-term with a satisfactory birth weight. There is no family history of IBD or immuno-deficiencies. She had presented with loose stools up to 10 times per day with mucus and blood streaks since 2 weeks old. She was initially diagnosed with cow’s milk protein allergy and was switched to an amino-acid based milk formula (Neocate). Despite 5 weeks of Neocate, she continued to have abnormal stools and poor weight gain. Blood tests revealed thrombocytosis (platelet 615 x 10^9/L), elevated ESR (74mm/Hr) and mild anaemia (haemoglobin 8.4g/dL). Endoscopy at 3 months revealed slough and multiple ulcers affecting the left colon and rectum. Histology
showed more than 100 eosinophils mainly in the lamina propria of the colonic biopsies. Test for cytomegalovirus was negative. Diagnosis of vEOIBD was made at 5 months when endoscopy was repeated as symptoms persisted. There was persistence of colonic ulcers and histology showed active chronic colitis with ulceration and a decrease in eosinophilic infiltrate. She has extra-intestinal features including intermittent oral thrush, vulva ulcer, peri-anal skin tags and eczema. Immunology work-up including lymphocyte subset, immunoglobulin levels, neutrophil oxidative burst test and IL-10R defect have returned normal. She has been started on prednisolone and azathioprine in the past 2 months with improvement. Evaluation for monogenic mutations is currently pending.

Conclusion: Eosinophilic infiltrate of the gastrointestinal mucosa may be an early manifestation of IBD. Patients should be closely followed up and a suspicion of IBD made if there is suboptimal response to typical therapy

P105. Pediatric Crohn’s disease and metastatic colorectal adenocarcinoma

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Introduction: Adult IBD patients are at increased risk of developing colorectal cancer; however, malignancy in young IBD patients is rare.

Aim: We present the case of a 15-year-old healthy boy, with no previous familiar history, who developed an invasive colon adenocarcinoma shortly after Crohn’s disease (CD) was diagnosed.

Methods: Patient presented to his local emergency unit with a 3-month history of abdominal pain, vomiting and weight loss. Further endoscopies and MRE were compatible with CD and induction of remission was attempted with exclusive enteral feeds. He was readmitted one week after with an acute abdomen and had ileal resection with ileostomy formation due to multiple small bowel perforations. Histology from resected bowel was in keeping with known CD. Patient suffered of a stormy post-operative course due to abdominal abscesses. He was commenced on Infliximab and Azathioprine with subsequently good progress, gaining weight and was discharged home.

Results: Two months later, patient was readmitted due to weight loss, anaemia and abdominal pain. He developed an acute bowel obstruction; laparotomy revealed multiple adhesions and a solid mass in small bowel which was resected. Histology and immunohistochemistry showed a metastatic adenocarcinoma poorly differentiated signet-ring type, likely to be primary gastric or colorectal (CK20+, CK7-, CEA+, chromogranin-, mismatch repair normal). Review of previous histology confirmed an inflammatory process but no malignancy. The primary tumour was later identified as an adenocarcinoma of transverse colon, metastases were only found in peritoneum (staging T4NkM1). Folfox chemotherapy (Folinic acid, Fluorouracil, Oxaliplatin) was commenced.

Conclusions: Malignancy should be considered as a differential diagnosis in PIBD when there is change in symptoms. Poorly differentiated adenocarcinoma is an extremely unusual finding in PIBD, and raises the possibility of an inherited familiar cancer syndrome or constitutional mismatch repair deficiency, which were both negative for our patient.

P106. Chronic recurrent multifocal osteomyelitis in children affected by inflammatory bowel disease

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INTRODUCTION Chronic Recurrent Multifocal osteomyelitis (CRMO) is a rare extra intestinal manifestation of Paediatric Inflammatory Bowel Disease (PIBD).

AIMS To describe a case series of PIBD patients with CRMO identified in our Centre.

METHODS We retrospectively reviewed all our PIBD patients between 2012 and 2016 using our database to identify patients with CRMO.

RESULTS: Four out of 321 PIBD patients(1.2%) had also CRMO, 3 females(F) 1 male(M), age range 8-12 years. Patient 1(F) presented with fevers and lower limb pain and was initially unsuccessfully treated with antibiotics for suspected infectious osteomyelitis. Whole body MRI and bone biopsy performed 6 months later showed signs of CRMO. Subsequently she developed abdominal pain and bloody diarrhoea and was diagnosed with ulcerative colitis(UC). Steroids and Azathioprine were started; due to steroid resistance treatment was escalated to Infliximab with remission of both UC and CRMO. Patient 2(M) presented with lower limb pain and increased inflammatory markers. CRMO was diagnosed with a lower limb MRI and treated with non-steroidal anti-inflammatory drugs. Twelve moths later he developed diarrhoea and abdominal pain. He was diagnosed with Crohn’s disease(CD) and treated with liquid enteral feeds(LEF) however didn’t receive immunomodulation, due to parental refusal and never achieved remission of CD and CRMO. Patients 3(F) and 4(F) presented with typical symptoms of inflammatory bowel disease and were diagnosed with CD. Whilst on treatment with LEF both developed lower limb pain and MRI showed signs of CRMO. Because of partial response to LEF, their treatment was escalated to Infliximab and Azathioprine leading to remission of both CD and CRMO.

CONCLUSIONS CRMO is a rare extraintestinal manifestation of IBD that may present before or after the onset of PIBD. Our case series has shown that once the underlying PIBD is treated appropriately the CRMO also resolves.

Keywords CRMO, MRI, Paediatric Inflammatory Bowel Disease
P107. Early onset inflammatory Colitis in a patient with Congenital Chloride Diarrhoea (CCD)

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Introduction and Aims: Congenital Chloride Diarrhoea (CCD) is a rare, autosomal recessive disorder caused by mutations in the SLC26A3 gene which encodes for a transmembrane chloride/bicarbonate ion exchanger mainly expressed in the apical brush border of the ileal and colonic epithelium. It is characterised by life-long, secretory, chloride-rich diarrhoea, and hypochloroemic, hypokalaemic metabolic alkalosis.

Material and Methods: We present the case of an 18-month-old female of non-consanguineous parents with genetically confirmed CCD and chronic, ulcerative pancolitis.

Results: The patient was noted to have polyuria, hyponatraemia, hypokalaemia, persistent metabolic alkalosis and elevated serum levels of renin/aldosterone in the first week of life, in the context of antenatal polyhydramnios. Renal causes were excluded. She was commenced on supplementary electrolyte therapy.

She represented at the age of seven months with vomiting and watery diarrhoea which progressed to bloody diarrhoea at the age of ten months. Faecal calprotectin was elevated (395 mg/kg, normal values<50 mg/kg).Colonic biopsies revealed chronic pan colitis with ulceration, empirically treated with oral steroids.

Further testing showed elevated faecal chloride of 116 mol/L and persistently high faecal calprotectin. Genetic testing confirmed the Down-Regulated in Adenoma (DRA) gene mutation, SLC26A3, which is diagnostic of CCD. Repeat endoscopy confirmed pan colitis with granulomas. This was treated with Azathioprine with positive clinical response.

Conclusions: This is, to our knowledge, the first reported case of CCD with concurrent colonic inflammation presenting under the age of two years. Early diagnosis and aggressive salt replacement therapy remain the mainstay of management in CCD to allow normal growth and to prevent associated morbidity and mortality. The clinician should, however, be aware of bowel inflammation as a potential cause of failure of conventional CCD therapy to control bowel symptomatology and the potential need for immunosuppression.

P108. Cutaneous manifestations of Pediatric Crohn’s disease

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Background: Paediatric patients with Crohn’s disease commonly present with dermatological disorders.

Aim: To document clinical features of clinical lesions of 5 children with CD referred for a dermatological opinion at a tertiary referral centre, and to review the literature for correlation between cutaneous lesions and CD.

Methods: Medical records of 5 children referred to the dermatology department were reviewed.

Results: 2 patients presented with single skin disorders and 3 patients presented with different forms of skin lesions. The dermatological disorders seen were recurrent sterile pustular rashes, erythema nodosum, oral and genital ulcers, pyoderma gangrenosum, psoriasis scalp inflammation and alopecia, erythematous patch with telangiectasia, and non specific blotchy rash affecting the upper body in one patient and the feet in another. 4 patients were on immunomodulators and one patient was on Infliximab.

Summary and Conclusion: A review of the literature shows that cutaneous disorders are associated with IBD are seen in up to 30% of children with CD, with erythema nodosum most frequently implicated. The diversity in the cutaneous lesions means that the treatment needs to be individualized. Skin disorders secondary to immunomodulators or Infliximab may improve with cessation of the offending drug although this will limit therapeutic options.

P109. Venous Thrombosis as a form of presentation in IBD - case report

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Background: Inflammatory bowel disease is associated with extraintestinal manifestations. Among these manifestations is the venous tromboembolism (VT) which presents a risk three times more than that in general population. Erythema nodosum is present in, about 5%, of children with Inflammatory Bowel disease.

Methods: We report the case of a 17-year-old male without prior medical history that came to the clinic for dermatologic lesions of erythema nodosum without history of gastrointestinal symptoms, such as, abdominal pain, chronic diarrhea and/or fever.

Results: Tuberculosis was ruled out and blood sample showed no anemia, leukocytosis or thrombocytosis, erythrocyt seimentation rate was normal and Protin C-reactive was negative. Fecal calprotectin was significantly high (775ug/g).

Abdominal Ultrasound showed thickness of terminal ileum, as did entero-MRI with a 50 mm length segment slightly thickened. Colonoscopy showed typical pattern of terminal ileum with serepiginous ulcers and “cobble-stone” pattern. Histologic findings were compatible with Crohn’s disease. The remainder of GI tract was spared.

Conclusions: The initial presentation at diagnosis was the venous thrombosis and, painful round inflammatory lesions, of the left lower extremity that resolved with the treatment of the the underlying disease.
P110. Exploring the role of PTPRT in the pathogenesis of VEO-IBD

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Background: We identified a patient diagnosed at 8 months with Crohn’s disease who also suffered from large joint arthritis. Whole Exome Sequencing (WES) identified compound heterozygous mutations in Protein Tyrosine Phosphatase, Receptor Type T (PTPRT). PTPRT is a phosphatase that acts downstream of the pro-inflammatory IL-6/JAK/STAT pathway by dephosphorylating STAT3. Interestingly, both JAK2 and STAT3 are present in loci associated with adult inflammatory bowel disease (IBD) by GWAS. The goal of this project is to validate the pathogenic role of PTPRT mutations in this VEO-IBD patient.

Methods: The interNational Early Onset Paediatric IBD Cohort Study (NEOPICS) collaboration aims to identify and investigate causes along with development of novel treatment for IBD in young children. Trio based WES identified rare damaging variants in PTPRT in this patient. One mutation (G411S) is in the extracellular fibronectin type III like (FN3) domain which is involved in cell-cell adhesion while the other mutation (Q791H) lies in the cytoplasmic juxtamembrane domain just upstream of the catalytic phosphatase domain. Peripheral Blood Mononuclear Cells (PBMCs) were isolated from the patient and unaffected parents and stimulated with IL-6 (10ng/mL) at various time points. Cells were harvested and lysed following stimulation and subjected to western blot analysis to measure pSTAT3 and STAT3 levels to quantify JAK pathway activation.

Results: Our PBMC assay show higher pSTAT3 levels at the 60 minute time point consistent with defective phosphatase activity in this patient.

Conclusions: Functional studies suggest impaired JAK-STAT3 deactivation in this patient due to the loss of PTPRT. Future ex vivo studies using patient derived cells will investigate if JAK tyrosine kinase inhibitors are effective at reducing the pSTAT3 levels. This personalized medical approach to control disease in this patient may also be applied to other patients with aberrant activation or impaired deactivation of JAK-STAT3 pathway.

Keywords: PTPRT, STAT3, IL-6, JAK
P111. Inflammatory Bowel Disease and Takayasu’s Arteritis an Association?

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Introduction
Inflammatory bowel disease (IBD) and Takayasu’s arteritis (TA) are disorders of chronic inflammation affecting the gut and vessels respectively. We look at a case of IBD and TA affecting the same patient; the diagnostic challenges this presented and association between the conditions.

Case A 17 year old male presented with weight loss, lower back pain and aching in the arms and legs. This was on a back ground of Crohn’s disease, diagnosed 5 years prior and controlled with infliximab. An endoscopy showed his Crohn’s was quiescent. On examination he had enlarged cervical lymph nodes and a patch of erythema on his left hand. He was extensively investigated as shown in table 1, before being diagnosed with TA.

Discussion: There are 62 case reports of TA and IBD suggesting a shared aetiology in the inappropriate activation of the immune system. Patients have a genetic susceptibility to TA and ulcerative colitis (UC) due to the presence of HLA-B52 and HLA-DR2. There are also non HLA genes linking both conditions including polymorphisms in the IL-12B gene.

In Crohn’s and TA, granulomata are seen; TNFα a cytokine key in the formation of granuloma plays an important role in aetiology of both conditions. Treatment with infliximab leads to remission in both conditions.

In TA autoantibodies are found against the aortic tissue and in IBD against the colonic mucosa. There are reports of these antibodies cross reacting. This might explain why patients with UC develop TA at a younger age than those without.

Conclusion Most patients with IBD will not develop TA but TA is easily missed in patients with IBD. It presents with similar symptoms including fever, malaise, weight loss and mesenteric ischemia causes gastrointestinal symptoms. TA should be considered as a differential in a patient with the above symptoms and a normal endoscopy.

P112. An unsolved case of a Very Early Onset IBD

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Background and objectives: Very-early-onset inflammatory bowel disease (VEO-IBD) may be caused by mutations in genes responsible for severe monogenic disorders. The identification of pathogenic genes by Next Generation Sequencing technologies could help clinicians to obtain a rapid diagnosis and specific therapies.

We report our experience of a VEO IBD male patient with a severe colitis phenotype, and a complicated disease course, unresponsive to medical and surgical therapy.

Methods: Retrospective case report.

Results: The patient presented Celiac disease and severe eating disorders. At 4 years old, onset of suspected UC (corticoresistant aspecific pan-colitis). He had Ciclosporine and azathioprine with complete clinical response for 5 months. Furthermore, he began Infliximab (7 doses), following azathioprine with partial response. At 5 years, he underwent to total colectomy with ileostomy, histology showed inflamation involving the limit of resection. After 3 months ileostomy bleeding with aspecific ileitis at biopsy. He started metronidazole, enteral nutrition and steroids with success. He became corticodependant: several attempting of tapering were followed by relapses. At 6 years old he had ileoanal anastomosis maintaining ileostomy. He continued steroids for 8 months, free of symptoms but developing Cushing Syndrome. Adalimumab with steroids withdrawn was started. After 4 doses, while he had only 3 mg/die of methylprednisolone, he relapsed. Metotrexate was added for 1 year and adalimumab was administered once a week with clinical response. At 7 years old, ileostomy was closed and continued adalimumab every 2 weeks. At first, the patient was studied for IL 10, IL 10 Rec Deficit, XLP, IPEX like, XIAP, anti-harmonin and villin antibody all negative. Subsequently whole exome sequencing was negative.

Conclusion: Distinguishing monogenic forms with a panel of candidate genes in VEO-IBD is a crucial importance to allow diagnosis and treatment. New gene undiscovered could help clinicians for unsolved intractable case of VEO IBD patients.
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