

7 weeks respectively. Nine (45%) had a good clinical response, 6 (30%) had a partial response, and 5 (25%) had no response; median SCAI at end of induction 0, 4 and 7 respectively. Colectomy rate at 1 year post IFX induction by response was 2/9 (22%) with a good response, 3/6 (50%) with a partial response, 5/5 (100%) for no response, with partial or no response significantly more likely to result in colectomy compared a good response ($p=0.02$). Overall, the colectomy rate for induction IFX at 1 year was 0.50 (10/20; 0.30 in 1st 3 months, 0.20 in months 4–12). Seven (35%) required CS at a median of 3 months (range 0–5) and 25% (5/20) a 2nd induction course of IFX at a median of 4.5 months (range 2–25) post IFX induction. Of these 5, 2 (33%) had a colectomy, 1 is receiving maintenance IFX, 1 had 3rd induction with IFX, 1 had an infusion reaction and commenced adalimumab. Following initial IFX induction, a further 26% (7/27) received maintenance IFX infusions, median 3 (range 1–6). Of these, 1 receives maintenance IFX, 3 stopped due to lack of funding and are in remission, and 3 (43%) lost response-requiring colectomy.

Conclusion Response to induction IFX determined by SCAI is useful in predicting colectomy in challenging UC patients with resistant or rapidly relapsing UC despite IS. Further induction or maintenance IFX is unlikely to result in remission with partial response on SCAI post induction IFX alone and in this group may be considered as a bridge to surgery.

Competing interests None declared.

REFERENCES

1. Rutgeerts P, et al. *N Engl J Med* 2005;**353**:2462–76.
2. NICE Guidance 163, 2008.

PMO-228 VITAMIN D DEFICIENCY IN A COHORT OF IBD PATIENTS TREATED WITH ANTI-TNF α THERAPY

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C R Parris, D R Gaya, J Winter, J Munro, A J Morris.* *Gastroenterology, Glasgow Royal Infirmary, Glasgow, UK*

Introduction There is a documented association between low Vitamin D levels and IBD. In addition to the metabolic effects of Vitamin D it also has an immunomodulatory role which includes inhibition of the Th1 response (IL-2, IL-10 and TNF- α). Vitamin D deficiency may be an effect of the inflammatory process resulting in malabsorption of Vitamin D from the gastrointestinal tract or a propagating factor in IBD through loss of Th1 suppression. Vitamin D deficiency may affect the response of IBD patients to biologic drugs that act through the same immunological pathway. The primary aim of this study was to determine the prevalence of Vitamin D deficiency in a cohort of IBD patients currently receiving biologic therapy and investigate whether levels were associated with disease activity as determined by the GI inflammatory marker, faecal calprotectin. The secondary aim was to determine if Vitamin D level was associated with the following parameters: treatment group, corresponding serum CRP, history of small bowel Crohn's, small bowel resection.

Methods Patients receiving infliximab or adalimumab therapy for IBD at Glasgow Royal Infirmary between 1 June and 31 July 2011 were included in this retrospective cohort study ($n=113$). The following patient information was extracted from the NHS Greater Glasgow and Clyde Clinical Portal Database: treatment regime, start date, underlying GI diagnosis, GI surgical history, previous biologic therapy, Vitamin D level (serum 25OHD) and corresponding serum CRP and faecal calprotectin.

Results 60 patients (53.1%) had a recorded Vitamin D level. Of these, 63.4% ($n=38$) were Vitamin D deficient (25 OHD <50 nmol/l); 21.4% ($n=13$) were severely Vitamin D deficient (25 OHD

<25 nmol/l). The median Vitamin D level of the active disease group (faecal calprotectin >200 $\mu\text{g/g}$) was 41 nmol/l (range: <14 –122 nmol/l) vs 39 nmol/l (range: 17–108 nmol/l) in the remission disease group (faecal calprotectin <200 $\mu\text{g/g}$), $p=0.63$. There were no significant associations between Vitamin D level and biologic treatment group ($p=0.65$), small bowel resection ($p=0.62$), history of small bowel Crohn's ($p=0.42$), and corresponding serum CRP ($p=0.33$).

Conclusion Significant Vitamin D deficiency is common in our cohort of IBD patients receiving anti-TNF α therapy. Vitamin D level appears to be independent of disease activity and other specified parameters. There is evidence to consider the routine measurement of Vitamin D levels in IBD patients receiving biologic therapy and appropriate treatment of Vitamin D deficiency.

Competing interests None declared.

PMO-229 MICRORNA EXPRESSION PROFILING IN STRICTURING CROHN'S DISEASE IDENTIFIES MIR-34A AS A FUNCTIONALLY RELEVANT INFLUENCE ON DISEASE PHENOTYPE

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¹A Nijhuis,* ²P Biancheri, ¹C Lai, ¹A Ghosh, ¹T Boitsova, ³C Chan, ²T MacDonald, ³J Lindsay, ¹A Silver. ¹Centre for Digestive Disease, Blizard Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK; ²Centre for Immunology and Infectious Disease, Blizard Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK; ³Digestive Diseases Clinical Academic Unit, Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK

Introduction Intestinal fibrosis is a frequent complication in Crohn's disease (CD), with subsequent stricture development that may require surgical intervention. MicroRNAs (miRNAs) are a novel class of post-transcriptional gene regulators implicated in cardiac, hepatic and pulmonary fibrosis. MiRNAs play a key role as modulators of the potent pro-fibrotic cytokine transforming growth factor (TGF)- β , which is up-regulated in CD intestinal strictures. Here, we aimed to identify and investigate the functional characteristics of miRNAs with differential expression between strictured and non-strictured CD.

Methods Intestinal surgical specimens were collected from 17 patients with fibrostenosing CD, and total RNA was extracted from uninflamed ileal mucosa. MiRNA expression profiling was performed using Illumina v2.0 microRNA array comparing matched strictured to non-strictured areas from the same patient within each experimental group. Subsequent validation of differentially expressed miRNAs was performed using qRT-PCR. Primary mucosal fibroblast cultures were derived from strictured CD and healthy control tissue. Overexpression of miRNAs was induced by transfection with Dharmafect agent under optimised conditions and changes in mRNA expression were detected by RT-qPCR and protein expression by IHC and Western Blotting.

Results We detected 11 miRNAs significantly up-regulated and 10 miRNAs significantly down-regulated (all $p<0.02$) between the strictured and non-strictured ileum. Validation experiments confirmed the changes of miR-34a in an independent set of 8 matched strictured vs non-strictured tissues. MiR-34a has been identified as a direct target of P53 which is involved in murine kidney fibrosis. When overexpressed in primary fibroblast cell lines, miR-34a increases expression of *COL1A2* and *COL3A1* mRNA in strictured CD cell line. However, upregulation of P53 mRNA or protein was not detected in 6 matched paired tissues, indicating a P53-independent mechanism by which miR-34a exerts its pro-fibrotic effects.

Conclusion This study confirms that differences in miRNA expression profiles between CD strictured and non-strictured areas can be detected. Upregulation of collagen mRNA shows that miR-34a might play a functional role in modulating fibrosis in CD, however further studies to investigate the impact of increased collagen protein are required. Manipulation of miRNA profiles may be a novel therapeutic strategy against fibrosis in Crohn's disease.

Competing interests None declared.

PMO-230 CLINICAL RISK FACTORS FOR CROHN'S DISEASE POSTOPERATIVE RECURRENCE ARE REFLECTED IN ALTERATIONS IN MUCOSALLY ADHERENT MICROBIOTA AT SURGICAL RESECTION

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^{1,2}A U Muruganathan,* ²D O Bernardo, ²P Tozer, ¹A L Hart, ²S C Knight, ³K Whelan, ¹N Arebi, ²H O Al-Hassi. ¹Gastroenterology, St Mark's Hospital, London, UK; ²Antigen Presentation Research Group, Imperial College, London, UK; ³Diabetes and Nutritional Sciences Division, King's College London, London, UK

Introduction Clinical risk factors for Crohn's disease (CD) recurrence after ileo-caecal resection (ICR) include smoking status, perforating disease and >1 surgical resection. The underlying mechanisms contributing to clinical risk are unknown. We aimed to study the relationship between risk factors and gut microbiota.

Methods Samples of macroscopically inflamed and non-inflamed small bowel from patients undergoing surgical resection for CD were analysed. Samples were snap frozen in liquid nitrogen. Cryosections were cut and the frozen sections were hybridised with oligonucleotide probes targeting the microbial 16S rRNA of total bacteria, *Escherichia coli*, *Bacteroides-Prevotella*, *Faecalibacterium prausnitzii*, *Clostridium coccoides-Eubacterium rectale* and bifidobacteria. The hybridised mucosa associated microbiota (MAM) were identified and quantified. Patients with ≥1 risk factor were classified as high risk for disease recurrence.

Results Fifteen patients underwent ICR (10 female); 9 were high risk (6 smokers, 4 fistulating disease and 2 recurrent resection- 3 patients had multiple risk factors). *Faecalibacterium prausnitzii* numbers in inflamed operative samples were lower in smokers compared with non-smokers ($p=0.036$). High-risk patients had lower numbers of bifidobacteria in both inflamed ($p=0.006$) and non-inflamed ($p=0.01$) operative samples compared with low risk patients.

Conclusion The risk of post-operative CD recurrence may be predetermined at a pre-operative stage due to dysbiosis. The role of MAM as a tool to stratify risk requires further study. Drugs that modulate MAM may, in future, play a role in reducing post-operative recurrence.

Competing interests None declared.

PMO-231 ILEAL AND COLONIC MUCOSAL DENDRITIC CELL CYTOKINE PROFILES DIFFER AT REST AND AFTER IN VITRO BACTERIA AND PRO-BIOTIC CHALLENGE IN POSTOPERATIVE CROHN'S DISEASE PATIENTS

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^{1,2}A U Muruganathan,* ²D O Bernardo, ²E R Mann, ¹C T Tee, ¹A L Hart, ¹N Arebi, ²S C Knight, ²H O Al-Hassi. ¹Gastroenterology, St Mark's Hospital, London, UK; ²Antigen Presentation Research Group, Imperial College, London, UK

Introduction Postoperative Crohn's disease (CD) recurrence predominantly affects the ileal mucosa at the ileo-colonic anastomosis with the colonic side often spared. Altered immune responses to bacterial flora are thought to be a driving force in the patho-

genesis of CD recurrence. Gut dendritic cells (DC) are key in the initiation of immune response, through cytokine production, when stimulated with bacterial antigens. We postulate that differences between ileal and colonic DC resting characteristics and functional responses may be responsible for the propensity of recurrence to occur at the ileal aspect of the anastomosis. We aimed to assess ongoing intracellular cytokine production in DC from ileal and colonic postoperative CD mucosa and assess their functional response to bacterial stimulation and modulation with probiotics.

Methods Paired ileal and colonic biopsies were taken from post-operative CD patients at colonoscopy ($n=11$). Lamina propria mononuclear cells were collected after collagenase digestion. DC intracellular cytokine responses (IL-2, IL-6, IL-17a, TGF β and INF γ) were assessed in basal conditions and after culture with LPS and two probiotic bacterial strains *Bifidobacterium Longum*; *Lactobacillus Casei* (*B longum* and *L casei*) using multi-colour flow cytometry.

Results Unstimulated ileal DC showed higher levels of ongoing intracellular production of pro-inflammatory cytokines than unstimulated colonic DC: IL6 (34.21 ± 12.80 vs 10.47 ± 3.574 cells/ μ l [mean \pm SEM], $p=0.037$), IL17a (24.62 ± 12.38 vs 14.94 ± 9.865 cells/ μ l, $p=0.05$, $n=5$) and TGF β (74.12 ± 17.96 vs 32 ± 16.27 cells/ μ l, $p=0.031$). Incubation with LPS resulted in higher DC intracellular cytokine levels of INF γ in ileal derived DC with a borderline p value (27.49 ± 12.61 vs 0.39 ± 0.391 cells/ μ l $p=0.06$) but not colonic derived DCs (19.55 ± 10.12 vs 12.40 ± 7.039 , $p=0.6$). *L casei* incubation, however, led to a larger decrease in ongoing TGF β (-42.35 ± 16.02 vs 4.42 ± 11.46 cells/ μ l $p=0.023$) and INF γ (-14.76 ± 7.196 vs 20.33 ± 10.16 cells/ μ l, $p=0.05$) DC cytokine production in colonic tissue compared with ileal.

Conclusion Ileal mucosa DC demonstrate a cytokine profile implicating a Th17 response compared with colonic mucosa. Upon bacterial stimulation with LPS ileal mucosa demonstrate increased INF γ DC production compared with unstimulated DC. These results suggest a role of for a Th1/Th17 response in driving post-operative CD recurrence. The probiotics *L casei* and *B longum* failed to show significant effects in modulation of intracellular cytokine production in ileal DC.

Competing interests None declared.

PMO-232 ABNORMAL LIVER FUNCTION TEST IN PATIENTS WITH ULCERATIVE COLITIS: A RETROSPECTIVE STUDY

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A A Thi,* K Holbrook, R Makins. Department of Gastroenterology, Cheltenham General Hospital, Cheltenham, UK

Introduction The association between primary sclerosing cholangitis (PSC) and ulcerative colitis (UC) is well recognised. The prevalence of PSC in patients with UC has been reported widely and ranges from 2.4% to 7.5%. The mean annual incidence rates were between 0.9 and 1.3 cases per 100 000 person years. Patients with UC may frequently be found to have abnormal liver biochemistry (LFTs) for numerous reasons although PSC is uncommon. Given the known increased risk of colorectal cancer in patients with both UC and PSC as well as cholangiocarcinoma, early recognition of PSC is crucial.

Methods Aims: To identify known patients with UC from our clinic population who also had persistently elevated LFTs and to determine the extent to which the cause of the abnormal LFTs had been investigated.

Methods A representative sample of patients with UC was identified from those who had contacted the nurse led IBD telephone help line at Gloucestershire Hospitals NHS Foundation Trust during September and October 2010. UC diagnosis was based on histology proven on biopsies including colectomy. Abnormal LFTs were defined as a persistent elevation above the local laboratory upper