in patients with inflammatory bowel disease on different biological therapy.

Results: In total, 387 respondents completed the questionnaire, and 47 participants (12%) developed COVID-19 infection. 66.9% of them were receiving anti-TNF inhibitor, 16.8% vedolizumab, 12.1% ustekinumab, and 4.1% tofacitinib. Based on our cohort, different biologic therapies didn't elevate the risk of infection (p=0.3486), nor the hospitalization rate (p=0.277). No one was in ICU or ventilator, and nobody passed away. Furthermore, 38.3% suspended the current biologic therapy, but it didn't decrease the rate of hospitalization (p=0.533), however, it didn't cause flare-ups either in the primary disease (p=0.415). Based on our cohort, neither vitamin supplementations meant protection against the infection (p=0.117), only regular mask wearing seems to protect patients with IBD (p=0.009).

Conclusion: Based on our cohort, more IBD patients develop the infection in Hungary, compared to international data, however, the outcome of the infection is more favourable. It seems, that the different biological treatments don't affect the infection rate, and neither elevates the hospitalization rate. In generally, there is no need to suspend the current biologic therapy, however, it should be a matter of individual judgment. After all, we claim that mask-wearing still seems to be the most effective form of prevention.

P667

Characterization of a large Hispanic cohort with Inflammatory Bowel Disease across a 25-year span

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Background: Inflammatory Bowel Disease (IBD) in Hispanics has increased, but characterization of this population is limited. We describe the demographic and clinical characteristics of a large Hispanic population with IBD and compare it among two periods, 1995- 2009 and 2010–2019.

Methods: The Registry of IBD has been recruiting patients with IBD continuously since 1995. Data is obtained from the subject and the medical record. This study includes 1365 Hispanics recruited between 1995 and 2019. Variables include age, gender, age at onset and diagnosis, IBD type, family history, smoking, extraintestinal manifestations (EIM), medications, and surgery for IBD. Descriptive statistics included frequency, median, mean, and standard deviation. SPSS software was used for comparison analysis utilizing Chi square and Fisher´s test. The protocol is approved by the IRB.

Results: 712 were males and 653 females. Crohn's disease (CD) was more prevalent in males (479/836, 57.3%) and ulcerative colitis (UC) in females (288/517, 55.7%). The mean age at diagnosis was 34.1 + 15.4 for UC and 24.4 + 12 for CD (p<.001). History of smoking was infrequent (24.3%). Interval between onset of symptoms and diagnosis was 1.8 + 4.7 yrs. for UC and 2.5 + 5.3 yrs. for CD (p=.012). At recruitment, duration of disease was 7.4 + 8.4 yrs. for UC and 5.6 + 7.3 yrs. for CD (p<.001). Family history of IBD was present in 23% of CD and UC participants. The most frequent EIM was arthropathy in 37.9% and 25.9 % of UC and CD (p=.670), followed by skin manifestations in 13.2% and 18.9% respectively (p=.070). Aminosalicylates (94.9%) and corticosteroids (81.6%) were more frequent in UC, and immunomodulators (23%) and anti-TNF drugs (aTNF) (46.2%) in CD (p<.001). At the time of recruitment, 54.5% of CD and 23.7% of UC patients had previous surgery for IBD.

Stratification of subjects into two groups by date of recruitment,1995–2009 and 2010–2019, showed similar ages at onset and diagnosis, but the time to diagnosis decreased for UC (2 vs 1.55 yrs.) and increased for CD (2.2 vs 2.6 yrs.) in the later interval. Medications varied between decades, with aTNF increasing markedly in CD and UC (p<.001) and aminosalicylates decreasing in CD (p<.001) in the later years. Surgery for UC decreased from 25.2% to 20.7%, whereas surgery for CD remained the same (52.2% vs 52.5%).

Conclusion: We describe a large cohort of Hispanics with IBD studied over two decades. Differences over time may reflect changes in disease phenotypes, environmental influences and the impact of physician awareness and new management guidelines and therapies. Further studies are needed to better characterize this population and explore outcomes.

P668

Does biotin deficiency play a role in the pathogenesis of Inflammatory Bowel Disease? Preliminary results of a cross-sectional study

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Background: Biotin, a water-soluble B-vitamin, has been shown to have anti-inflammatory properties. A biotin-deficient diet was recently shown to induce a colitis-like phenotype in mice, alleviated by biotin substitution. Mice with DSS colitis showed biotin deficiency and significantly reduced levels of SDMT, a protein involved in biotin absorption. Oral biotin substitution reversed DSS colitis and induced remission by inhibiting NF-κB, a transcription factor that hinders inflammatory cytokine expression and plays a role in intestinal barrier integrity and IBD. We investigated for the first time a possible clinical role of biotin status in IBD.

Methods: In a comparative, cross-sectional study, serum samples of IBD patients were compared with samples of 80 healthy blood donors (40f;18-65y). CBC, albumin and hsCRP were determined by standard tests and samples assessed for presence/absence of inflammation (serum hsCRP, cutoff <5mg/L). Since its known that serum biotin levels does not accurately reflect biotin status, serum 3-hydroxyisovaleryl carnitine (3HIAc) levels were determined by LC-MS/MS.

Results: 138 IBD patients (67f;72 CD/66 UC;42.5±14.3y) were enrolled. Of these, 83/138 had inflammation (39f;43CD/40UC;42.5±14.6y) and 55/138 no inflammation (28f;29CD/26UC;42.5±13.9y). In IBD patients, mean serum 3HIAc levels were significantly higher vs. controls but similar with vs. without inflammation (Table 1). The reference serum 3HIAc level

was calculated as 11.0–27.3 nmol/L from controls; biotin deficiency was defined as >27.3 nmol/L 3HIAc (90thPC), since no validated cut-off exists. Biotin deficiency in IBD patients was significantly greater than in controls (Table 1).

Conclusion: High serum 3HIAc levels were associated with IBD. In line with preclinical studies, biotin deficiency was more pronounced in IBD patients than controls. No relation was found with inflammatory activity or disease type. Our findings suggest that biotin may have a bigger role than thought in IBD; whether as a cause or effect in IBD pathogenesis warrants investigation. Routine assessment and correction of biotin status may ameliorate IBD and help maintain intestinal integrity.

Table 1: 3-hydroxyisovaleryl carnitine levels and biotin deficiency

c	IBD Patients			p_1	Controls (n=80)	p_2
	Inflammatory (n=83)	Non-inflammatory (n=55)	Total (n=138)			
3HIAc [nmol/L] Median [range]	20.0 [5.8-79.4]	20.6 [7.2-59.2]	20.1 [5.8-79.4]	0.731	17.3 [7.0-42.6]	0.024*
Biotin deficiency N[%]	25[30.1]	16[29.1]	41[29.7]	0.897	7[8.8]	<0.001**

p_1: statistical significance, inflammatory vs. noninflammatory patients, p_2: statistical significance, IBD patients vs. controls
*p<0.05, **p<0.001 (3HIAc; Mann-Whitney U test. Biotin deficiency; chi^2 test)

Genetics

P669

Effect of vedolizumab therapy on whole blood transcriptional profiles in patients with Inflammatory Bowel Disease

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Background: Vedolizumab (VDZ) is one of many new biological drugs used in patients with inflammatory bowel disease who fail more conventional therapy. Despite proven efficacy, subgroups of patients show limited clinical benefit from VDZ. Here, we hypothesized that differences in clinical response to VDZ therapy might be reflected in changes in gene expression in whole blood which potentially could serve as easy accessible candidate biomarkers.

Methods: Transcriptional profiles of 20 patients (Crohn's disease 13, ulcerative colitis 7) were established by sequencing of RNA isolated from stabilized whole blood collected at baseline (T0), and at follow-up at week 10–12 (T1) following three infusions of VDZ. Clinical response was defined as a decrease of > 3 in the simplified Harvey Bradshaw Index or in the Simple Clinical Colitis Activity Index at T1 compared with T0. Differently expressed genes were identified by using the R packages Rsubread, edgeR and limma with hg38 as reference genome. Pathway analyses were done by gene set enrichment analysis (GSEA, Broad Institute) using Reactome and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways. Routine laboratory parameters were obtained.

Results: Overall, two genes were down-regulated (*IGLV2-23* > 2-fold) and four genes were up-regulated (*ADAMTS5* > 2-fold) at follow up (FDR < 0.05). This was attributed to regulation in responders (n=9), but not in non-responder (n=11). In responders, 55 genes were down-regulated (25 genes > 2-fold, *e.g. IGHV3-74*) and 146 genes were up-regulated (8 genes > 2-fold, *e.g. OLFM1*) at T1 *vs.* T0. However, at T0 there were no differences between responders and non-responders suitable as predictive biomarkers. Nevertheless, 89 KEGG pathways were differently enriched between study groups at baseline, and up to 44 pathways within the groups when studying the transcriptional profiles over time (FDR < 0.075). The plasma-concentration of VDZ was not associated with the clinical outcome, and was not correlated with the dose of VDZ (mg/kg bodyweight).

Conclusion: There is a strong need for reliable and predictive biomarkers in decision making for personalised medicine. Our study shows that VDZ affects the transcriptional profile in blood of patients responding to treatment, whereas no gene regulation was noticed in non-responders. It also suggests that whole blood is not optimal for identifying predictive pre-treatment biomarkers based on individual genes in patients with need for this integrin inhibitor. However, treatment outcome may depend on several interacting genes, illustrated by the identification of significant pathway differences between study groups, both at baseline (T0) as well as in response to treatment (T1). Further studies are needed to confirm our findings.

P670

Identification of two additional susceptibility loci for Crohn's disease in Koreans

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Background: Genome-wide association studies (GWAS) have identified more than 240 susceptibility loci associated with IBD mainly in Caucasians, however, there are limited studies in other populations.

Methods: To identify additional susceptibility loci in Asians, we expanded our previous study design (comprising a total of 1,621 patients with Crohn's disease [CD] and 4,419 controls), followed by replication in an additional 582 patients with CD and 845 controls. To determine biological processes associated with candidate genes for CD, we conducted pathway analyses by MAGMA using the results obtained through the current meta-analyses and the summary statistics of the largest meta-analysis in the European population as input.

Results: The meta-analysis of Korean GWAS identified two novel susceptibility loci for CD at rs2240751 in the *MFSD12-C19orf71-FZR1-DOHH* region on 19p13 ($p_{combined} = 3.03 \times 10^{-8}$) and rs6936629 in the *RFX6-GPRC6A-FAM162B* region on 6q22 ($p_{combined} = 3.63 \times 10^{-8}$), of which rs6936629 showed significant association in European population ($p = 1.88 \times 10^{-4}$). Comparisons of the top 10 pathways for CD between the Korean and European data showed that MHC class II protein complex, antigen binding, and response to antigenic stimulus-related pathways were more significant in the Korean population (Figure 1A), whereas cytokine and transcription factor-related pathways were more significant in the European population (Figure 1B).