#58 - PREVALENCE IN A CHILEAN IBD COHORT OF GENETIC RISK VARIANTS ASSOCIATED TO ADVERSE EVENTS TO THIOPURINES.

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Background:Thiopurines are commonly used treatments for patients with Inflammatory Bowel Disease (IBD) in Chile. However, thiopurines can induce adverse events (AEs) such as myelotoxicity and pancreatitis. Genetic variants have been identified that increase the risk of these AEs, including variants in the nudix hydrolase-15 (NUDT15) and Thiopurine-S-methyltransferase (TPMT) genes, which are involved in thiopurine metabolism and related to myelotoxicity. Objective. To evaluate the prevalence of genetic variants and risk alleles associated with AEs to thiopurines in Chilean IBD patients and compare their frequencies with those in other populations. Method. We genotyped 192 IBD patients using Illumina screening array for 725,497 single nucleotide polymorphisms (SNPs). We identified SNPs associated with thiopurine AEs in IBD patients by searching the GWAS catalog and then looked for these SNPs among the genotyped Chilean IBD patients. Results. A total 20 SNPs were identified in the GWAS catalog. We found that only four genetic variants were present in our cohort. The three variants related to myelotoxicity had infrequent risk alleles, which suggests that these variants may not be major contributors to myelotoxicity in Chilean IBD patients. However, the prevalence of the risk allele rs6935723-C for pancreatitis was relatively high at 0.33 (Table 1). Conclusion:Our study sheds light on the prevalence of genetic variants linked to thiopurine-induced adverse events in Chilean IBD patients. Frequencies of these variants vary among different populations, which may have implications for the use of thiopurines in different ethnic groups. Genetic testing may be useful in identifying patients who are at risk for thiopurine-induced pancreatitis and could help guide treatment decisions. Further research is needed to confirm and explore the clinical implications of genetic testing in this population.

Table 1.Frequency of Variant and risk allele related to Thiopurines adverse events in IBD Chilean patients

Variant and risk allele	Chr	Allele Frequency	Mapped gene	Reported trait	Genotype		
rs116855232-T	13	C=0.94 T=0.06	NUDT15	Thiopurine-induced leukopenia in inflammatory bowel disease	CC 0	TC 22(11.5%)	TT 170(88.5)
rs79206939-A	16	A=0 G=1	FTO	Thiopurine-induced leukopenia in inflammatory bowel disease	AA 0	AG 0	GG 192(100%)
rs1142345-G	6	G=0.03 A=0.97	TMPT	Thiopurine methyltransferase activity in acute lymphoblastic leukemia patients treated with mercaptopurines	GG 0	GA 13(7%)	GG 178(93%)
rs6935723-C	6	C=0.33 T=0.67	HLA-DQB3, MTCO3P1	Response to thiopurine, thiopurine immunosuppressant-induced pancreatitis	CC 26(13.5%)	CT 101(52.6%)	TT 65(33.9%)

References. References 1. GWAS catalog 2.Ensembl.org