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Several genetic SNPs identified in acute appendicitis patients including the HLA-C known to be related to coeliac disease in a Genome-Wide Association Study

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Acute Appendicitis (AA) is an inflammatory condition of the vermiform appendix in the caecum of the colon. Genetic polymorphisms have been suggested as risk factors predisposing to AA susceptibility but have remained relatively unknown, due to insufficient sample size in previous analyses. Therefore, the primary research aim was to identify genetic variants associated with AA. It was hypothesised that gene polymorphisms associated with AA will provide a connection to other diet-related inflammatory diseases. Genetic variants associated with AA were studied via a Genome-Wide Association Scan (GWAS) using the Global Biobank Meta-Analysis Initiative (GBMI). The GBMI is a collaborative consortium of 23 biobanks with a publicly released repository of de-identified genetic data linked with digital health records spanning 4 continents with a study population size of over 2.2 million consented individuals of multiple ancestral backgrounds[1]. A linear regression model was used to estimate the association between single nucleotide polymorphisms (SNPs), across the human genome, and AA by each contributing biobank. The results were then meta-analysed with a total of 32,706 cases and 1,075,763 controls. In the present study, the free open-source Complex Traits Genetic Virtual Lab (CTG-VL) platform was used to access, analyse, and visualise the GWAS summary statistics of AA[2]. Genome-wide significantly associated SNPs (p-value < 5×10^{-8}) were further searched for their associations with health-related traits in publicly available GWAS summary statistics. Upon analysis, significantly associated SNPs for AA were identified within or nearby nine genes. *HLX*, *NKX2-3*, *LTBR*, and *DLEU1* are genes involved in immune responses; IRF8 associated with maturation of myeloid cells; OSR-1 responsible for transmembrane ion transporter activity; NCALD a regulator of G protein-coupled signal transduction. In addition, based on the hypothesis, the SNP of key clinical importance was the *HLA-C* rs2524046 (p-value = 2.38×10^{-8}), with the AA risk-increasing allele C being also strongly associated with a higher risk of coeliac disease (CD). The CD is an autoimmune condition where gluten, a protein present in grains such as barley, rye, and wheat, elicits an inflammatory response that results in damage to the small intestine lining. Considering how both AA and CD share the same SNP, it is possible to speculate whether gluten initiates a similar pathophysiological mechanism that exacerbates inflammation in the vermiform appendix in AA. In conclusion, the top AA associated SNPs suggests its development could be due to immunological responses influenced by dietary nutrient intake. The HLA-C SNP is common to AA and CD, suggesting that the gluten protein found in certain cereal grains possibly contributes to the pathophysiology of AA like CD. This warrants further investigations into whether dietary gluten could play a key role in AA development.

Keywords: acute appendicitis; coeliac disease; genome wide association study; single nucleotide polymorphism

Ethics Declaration

Yes

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