COMMENTARY

Inflammatory bowel illness is associated with altered gut bacterial and metabolic profiles, as well as their interplay

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ABSTRACT

The gut microbiome's dysregulation has been linked to the development of numerous illnesses. Using data from the Human Microbiome Project (HMP) and the Integrative Human Microbiome Project, this study investigated the role of microbial and metabolic signatures, as well as their interaction between patients with Inflammatory Bowel Disease (IBD) and Healthy Controls (HCs), using a combination of machine learning and traditional statistical analysis (iHMP). The microbiological and metabolic fingerprints of IBD patients were found to be considerably different from those of healthy controls. IBD sufferers had 25 enriched species and 6 deficient species as compared to HCs. In addition, 17 differentiating pathways were discovered between the IBD and HC groups. These distinct pathways were mostly engaged in amino acid, nucleotide, and carbohydrate production and breakdown. The non-predominant bacteria Ruminococcus obeum and the predominant bacteria Faecalibacterium prausnitzii created the same wide and strong co-occurring interactions with pathways, according to co-occurrence network analysis. Furthermore, the study discovered a panel of combinatorial markers that might identify IBD from HCs. The model's excellent accuracy (AUC=0.966) and efficacy were validated by Receiver Operating Characteristic (ROC) and Decision Curve Analysis (DCA). Meanwhile, external validation using an independent cohort revealed the same excellent effectiveness (AUC=0.835). These findings suggest that gut bacteria may play a role in IBD aetiology and pathophysiology, and that they might be used as a non-invasive diagnostic tool in the future.

Key Words: *Inflammatory bowel disease; Gut microbiome; Metabolic pathways*

INTRODUCTION

IBD is a debilitating and multifactorial complex illness defined by anomalies in the immune system, intestinal homeostasis iss--ues, and alterations in gut microbiota. It is the most prevalent complication in adults, covering both Crohn's Disease (CD) and Ulcerative Colitis (UC). In IBD patients, periods of clinical remission and illness flare-ups are common, and they have a significant impact on survival and quality of life. Although various ideas have been proposed to explain IBD's pathophysiological processes, the fundamental biological foundation of the disease remains mostly unknown. However, mounting data shows that the gut microbiota plays an important role in the development and treatment of IBD: In animal models of chronic intestinal inflammation, being germ-free reduces the severity of symptoms; in humans with IBD, reactivity to intestinal microbes has been altered; and antibodies in the blood are a well-known biomarker in CD and UC, but antibodies are only present when the intestine microbiota has been altered. Although the exact origin of IBD is unknown, efforts to reduce microbiota exposure (such as elemental diets or antibiotic medication) can help with certain forms of the disease.

Metagenomics datasets generated by the HMP and iHMP were employed in the study to look into the function of microbial and metabolic markers, as well as their interaction with the IBD and HCs. Furthermore, data was gathered to highlight the association between particular microbial composition, abundance, and metabolic pathways, as well as how IBD severity was regulated, either directly or indirectly, by modifying the gut microbiota, using co-occurrence network analysis. Furthermore, a risk classification method involving machine-learning algorithms was proposed to assess IBD risk based on the biological significance and accuracy contribution of the bacterial genus in the cohort, and the accuracy of the model was further verified using an external independent cohort, which showed the same high accuracy. This study highlighted the landscapes and interaction networks of various microbes and pathways in the IBD and HCs groups, as well as a unique approach called HADRCM, which is based on machine learning and statistical analysis. Meanwhile, utilizing HADRCM, a combinatorial marker panel capable of accurately distinguishing IBD from HC participants was found and independently confirmed, and the model's nomogram could be used in clinical practice.

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Furthermore, because the two subtypes of IBD (CD and UC) have distinct microbial communities, this theoretically-based technique may be used to differentiate IBD subtypes. Our findings imply that gut microbiota disruptions may play a role in IBD pathogenesis by influencing the host's amino acid, nucleotide, cofactor, vitamin, and carbohydrate metabolism, opening up a new window into the disease's origins.

Metagenomic sequencing, as opposed to 16s rRNA amplicon sequencing, can give species-level and more important information, particularly putative functional processes in the microbiota. Our findings were similar to a prior study, which found a reduction in alpha diversity in IBD patients but did not specify the species level. There were 25 distinct bacterial species found to be responsible for this discrimination, the majority of which were from the phyla Firmicutes (72.2%), but there were also deficient species from the phyla Bacteroidetes (55 percent). The findings of this study corroborate earlier reports of alterations in the phyla Firmicutes and Bacteroidetes in IBD patients compared to HCs. Bacteroidetes play an important role in the interactions between the gut microbiota and the host, particularly in metabolic pathways. Many Bacteroides species were substantially connected to the amino acid, nucleotide, cofactor, vitamin, and carbohydrate metabolism, which is consistent with earlier results.As a result, reduced amino acid levels in IBD may be due to Bacteroides species downregulation. Faecalibacterium prausnitzii was shown to have significant co-occurring interactions with several pathways related to carbohydrate and amino acid metabolism in the co-expression network analysis, and it was the dominating species in both categories. In addition, past gut microbiome research has revealed that Faecalibacterium has unique impacts on IBD. Faecalibacterium prausnitzii was shown to have significant co-occurring interactions with several pathways related to carbohydrate and amino acid metabolism in the co-expression network analysis, and it was the dominating species in both categories. In addition, past gut microbiome research has revealed that Faecalibacterium has unique impacts on IBD. Machine learning is becoming more popular in the realm of illness diagnosis. Many research, on the other hand, just use a single method or rudimentary statistics, resulting in low accuracy. It's also uncommon and difficult to use in genuine clinical medical diagnosis. In this work, the diagnostics model was built using a combination of random forest, logistic regression, and statistical analysis, and the great performance was validated using ROC and DCA. HADRCM was created by combining the approaches. Some microbial indicators might successfully distinguish IBD patients from HCs using HADRCM. Furthermore, in an independent external cohort, a combinatorial marker panel could differentiate IBD individuals from HCs with an AUC of 0.966, while still generating a strong performance with an AUC of 0.835. Finally, this output nomogram can give doctors non-invasive diagnostic proof. As a result, the HADRCM might be a viable option in a cohort research.