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INPLASY

Alistipes depletion is a general feature of ucler colitis patients — A meta-analysis based on 1992 individuals

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ADMINISTRATIVE INFORMATION

Support - No.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 October 2024 and was last updated on 15 October 2024.

INTRODUCTION

Review question / Objective In this study, we downloaded and reanalysed the raw data from published articles from NCBI, expecting to find biomarkers related to ulcerative colitis by exploring the gut microbial characteristics of normal people and UC patients in the overall population and in different geographical areas. We also explored whether the gut microbiota of UC is geographically specific and the commonalities and differences between them.

Rationale Clinical studies involving patient cohorts are the primary method for discovering biomarkers. However, these studies face significant challenges related to sample size, sequencing technology diversity, and other variables. Such variability can result in substantial differences in quantitative metrics, leading to seemingly contradictory findings. To address these issues, meta-analysis offers a valuable approach, not only mitigates the limitations of individual studies but also enhances the robustness and generalizability of findings through statistical aggregation. However, it is important to note that meta-analyses primarily rely on literature-derived data compiled by researchers, rather than original raw data. This limitation can affect the depth and precision of the analysis, as direct use of raw data could provide more comprehensive and accurate insights. Fortunately, clinical studies of gut microbiota require raw sequencing data to be uploaded to a public network, which allows us to access the microbiota data of each study participant and to aggregate and re-analyse information from patients in different countries and study cohorts. Such efforts would enable more accurate identification of gut microbe that are closely related with UC and deepen our understanding of the role of gut microbes in UC pathogenesis.

Condition being studied Ulcerative colitis (UC) is a chronic, non-specific inflammatory disease primarily afffecting the mucosal lining of the large intestine, particularly the rectum and sigmoid region . The disease is characterised by the formation of multiple, contiguous ulcers in the mucosa, leading to symptoms such as abdominal pain, frequent diarrhoea and significant alterations in bowel habits. The global incidence of UC is increasing, particularly in economically developed regions like North America and Europe . While the incidence and prevalence of UC vary widely across geographical regions, the global incidence ranges from 98 to 233 cases per 100,000 individuals.

METHODS

Search strategy Literature was searched in Pubmed, Cochrane library and Web of Science databases for keywords (ulcerative colitis OR UC) AND (gut microbiome OR gut microbiota OR gut bacteria) before 1 March 2024.

Participant or population We downloaded the original sequences of 16S rRNA and the corresponding grouping information from the NCBI website under the bioproject,and then used the plug sratookits in ubuntu to split the original sequences into one or two sequences, and used the fastqc plug to carry out quality control, and then used the dada2 plug of qiime2 (https://docs.qiime2).

Intervention Doctors diagnosed the disease as ulcerative colitis, with the formation of several consecutive ulcers on the mucous membranes, which manifested themselves in the form of abdominal pain, frequent diarrhoea and a marked change in the bowel habit.

Comparator People without ulcerative colitis who have not taken antibiotics and probiotics in the last three months.

Study designs to be included We reanalyze the gut microbiota of 1,148 UC patients and 844 HC individuals to characterize the gut microbiota of UC patients, focusing on those from different regions.

Eligibility criteria Inclusion and exclusion criteria
Inclusion criteria: ①research subjects are human; ②cohort study; ③research article; ④sequencing method is 16S rRNA.
Exclusion criteria: ①object of concern is the animal; ②pregnancy or lactation, diabetes mellitus, cancer or other systemic or serious diseases; ③use of antibiotics, probiotics or faecal transplants in the past 3 months, history of colorectal surgery, persistent or recent infectious colitis in the included subjects; ④no raw data or unclear grouping of raw data.

Information sources Literature was searched in Pubmed, Cochrane library and Web of Science databases for keywords (ulcerative colitis OR UC) AND (gut microbiome OR gut microbiota OR gut bacteria) before 1 March 2024.

Main outcome(s) Based on 1992 individual data, our findings reveal that UC patients exhibit significantly lower species richness and diversity compared to healthy individuals, with notable geographic variations. The genera Alistipes, Phascolarctobacterium, Bilophila, and Coprococcus consistently showed reduced abundance in UC patients across all populations. Notably, Alistipes emerged as a key biomarker capable of differentiating UC patients from healthy controls globally, while Blautia displayed high predictive value specifically within North American cohorts.

Additional outcome(s) Notably, Alistipes emerged as a key biomarker capable of differentiating UC patients from healthy controls globally, while Blautia displayed high predictive value specifically within North American cohorts. This systematic analysis revealed the microbial characteristics of patients with UC and its variation across geographic regions, a finding that provides a solid scientific basis for diagnostic and therapeutic strategies for UC.

Data management Both raw data and intermediate files of the data processing process are kept.

Quality assessment / Risk of bias analysis The quality of the included literature was assessed using the Newcastle-Ottawa Scale (NOS), which consists of three main dimensions: Selection, Comparability, and Outcome. The total score of the NOS is 9 points. Higher scores indicate higher study quality, with NOS scores of 1-3, 4-6, and 7-9 defined as low, medium, and high quality, respectively. When the heterogeneity was low ($I2 \leq 50\%$), a fixed-effects model was used; when the heterogeneity of the results was high ($I2 > 50\%$), the source of heterogeneity was further analysed, and a random-effects model was used after eliminating the influence of obvious heterogeneity. Obvious heterogeneity was dealt with by subgroup analysis or Egger's sensitivity analysis.

Strategy of data synthesis Meta-analysis of the included literature was performed using Stata15 software. Information on continuous variables was used as standardised mean difference (SMD) as an effect indicator. The results of the included studies were analysed by the heterogeneity test. Heterogeneity methods are provided in the Appendix Supplementary 3. The test level for meta-analysis was statistically significant at $P<0.05$. The study subjects were divided into different subgroups according to the region where they were located. The analyses of alpha diversity, beta diversity, and STAMP differences in the gut microbiota of normal subjects and UC patients, both overall and within the subgroups, were performed using the wilconxon test.

Subgroup analysis The I2 value for Europe, North America, Asia, China, and the United States were 77.7%, 50.8%, 91.8%, 49.7%, and 64.6%, respectively, suggesting that geography may be a key factor contributing to heterogeneity. Therefore, all subsequent analyses of gut microbiota in healthy individuals and UC patients were conducted both globally and regionally.

Sensitivity analysis Tthe combined effect value of the Shannon index was -0.65, with a 95% confidence interval of -0.92 to -0.38, and $I2 = 84.3\%$, $P < 0.05$. However, the I2 value exceeding 50%, along with a significant p-value, indicated heterogeneity among the included studies. A subsequent sensitivity analysis revealed that removing any one cohort arbitrarily resulted in confidence intervals of -0.75 to -0.38 for the remaining 36 cohorts (Figure 2B), suggesting that the literature selection was not responsible for the observed heterogeneity.

Language restriction No.

Country(ies) involved China.

Keywords Ulcerative colitis (UC); gut microbiota; biomarker.

Contributions of each author

Author 1 - Jiale Cheng - Jia-Le Cheng conducted the database searches, raw data analysis, interpretation of the results and wrote the first draft of the manuscript, and evaluated the risk of bias of the included studies, evaluated the quality of evidence.
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Author 2 - Yanan Yang - Ya-Nan Yang evaluated the risk of bias of the included studies, evaluated the quality of evidence.
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Author 3 - Chongming Wu - Chong-Ming Wu conceived the study idea and designed the study. Jia-Le Cheng conducted the database searches, raw data analysis, interpretation of the results and wrote the first draft of the manuscript. Chong-Ming Wu made substantial contributions to the critical revision of the manuscript.
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