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Letter to the editor

Can gut microbiota explain acute diverticulitis occurrence in patients with symptomatic uncomplicated diverticular disease?

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Why patients with symptomatic uncomplicated diverticular disease (SUDD) may develop acute diverticulitis (AD) is still unknown. We analyzed the gut microbiota (GM) in two SUDD patients, one who did experience SUDD recurrence but not AD occurrence (case 1) and one who did experience AD occurrence during follow-up (case 2). The GM of these patients showed differences in terms of phyla (Firmicutes and Bacteroidota in case 1; Actinobacteriota and Proteobacteria in case 2) and subgenera (*Prevotella* and *Phascolarctobacterium* in case 1 and *Alloprevotella*, *Prevotella*, *Holdemanella*, *Turicibacter*, *Eubacterium eligens* group, and *Dialister* in case 2). This novel insight may advance our ecological understanding of this complex disease.

Key words: acute diverticulitis, symptomatic uncomplicated diverticular disease, gut microbiota

TO THE EDITOR

Diverticulosis of the colon, the most frequent anatomic alteration in adults aged 70 years or older in the western world [1], may become symptomatic, developing the so-called symptomatic uncomplicated diverticular disease (SUDD). Although it occurs in up to 25% of patients having diverticulosis [2, 3], it is not well understood yet why patients having SUDD may develop the occurrence of acute diverticulitis (AD).

Recent studies found that microbiota perturbations may be found in SUDD [4–6] and in AD patients [7–9]. However, no data are currently available about potential differences in gut microbiota (GM) between SUDD patients developing or not developing AD.

We retrospectively assessed SUDD patients who had stool samples collected by fecal swab for microbiological studies and stored in the Unit of Microbiome Science and Biotechnology, Department of Pharmacy and Biotechnology, University of Bologna (Bologna, Italy). We identified two patients, one having SUDD recurrence and one having AD occurrence after diagnosis of SUDD.

The gut microbiome in the SUDD patient with SUDD recurrence (case 1, an 81-year-old man, Fig. 1a) but without AD occurrence showed interesting characteristics. In particular, the abundances of the Firmicutes and Bacteroidota phyla, the very low presence of the phyla Actinobacteriota and Proteobacteria, the abundances of *Bacteroidaceae*, *Lachnospiraceae*, *Ruminococcaceae*, *Prevotellaceae*, *Peptostreptococcaceae*, and *Acidaminococcaceae* represented a mature GM, typical of adult people [10]. On the contrary, the overexpression of several mucin-degrading taxa, such as *Roseburia*, and *Faecalibacterium* confirmed that this overexpression may be a typical microbial fingerprint in SUDD [7–9] and that it differs from that occurring in inflammatory bowel disease (IBD) [11]. Finally, the overexpression of *Prevotella*, which is considered a commensal bacteria able to trigger the occurrence of rheumatoid arthritis [12], and *Phascolarctobacterium* confirmed the complex interaction among the bacteria in SUDD, which needs to be better understood [13].

The gut microbiota analysis of SUDD patient in whom AD occurred (case 2, a 51-year-old man, Fig. 1b) showed abundance of Actinobacteriota and Proteobacteria phyla, very low represented in SUDD patient with no AD occurrence, and already associated with risk of IBD [11]. Moreover, the family *Bacteroidaceae*, the members of which are considered protectors against some autoimmune diseases [14], was underrepresented in this patient. *Prevotellaceae*, *Erysipelotrichaceae*, and *Veillonellaceae*, which are strictly linked to the severity of IBD

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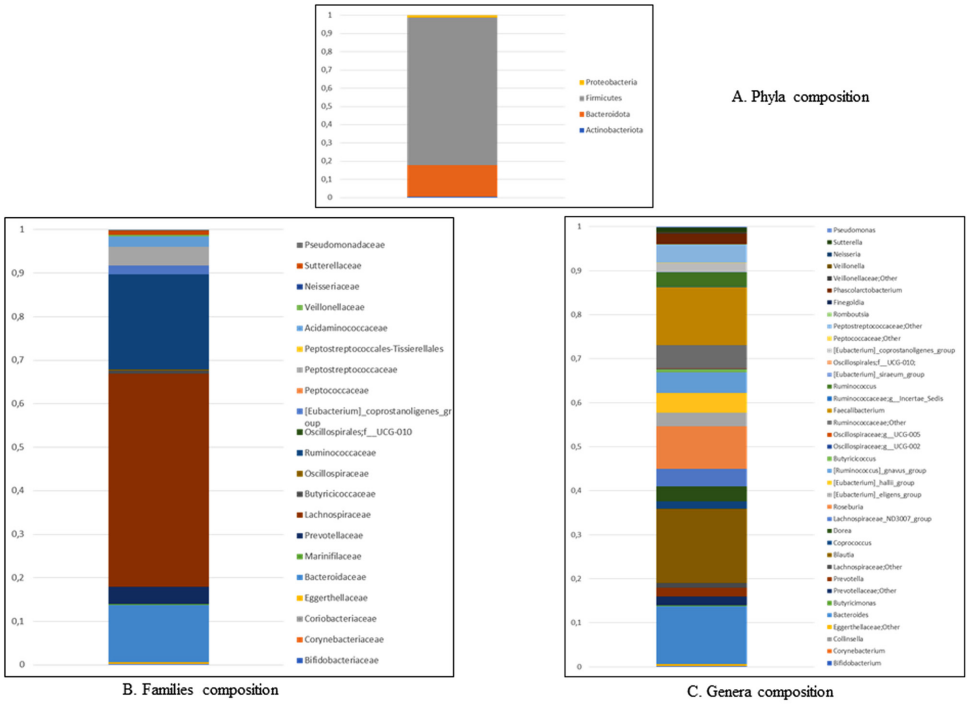
1a. Gut microbiota in SUDD patient without AD occurrence (case 1).



1b. Gut microbiota in SUDD patient with AD occurrence (case 2).

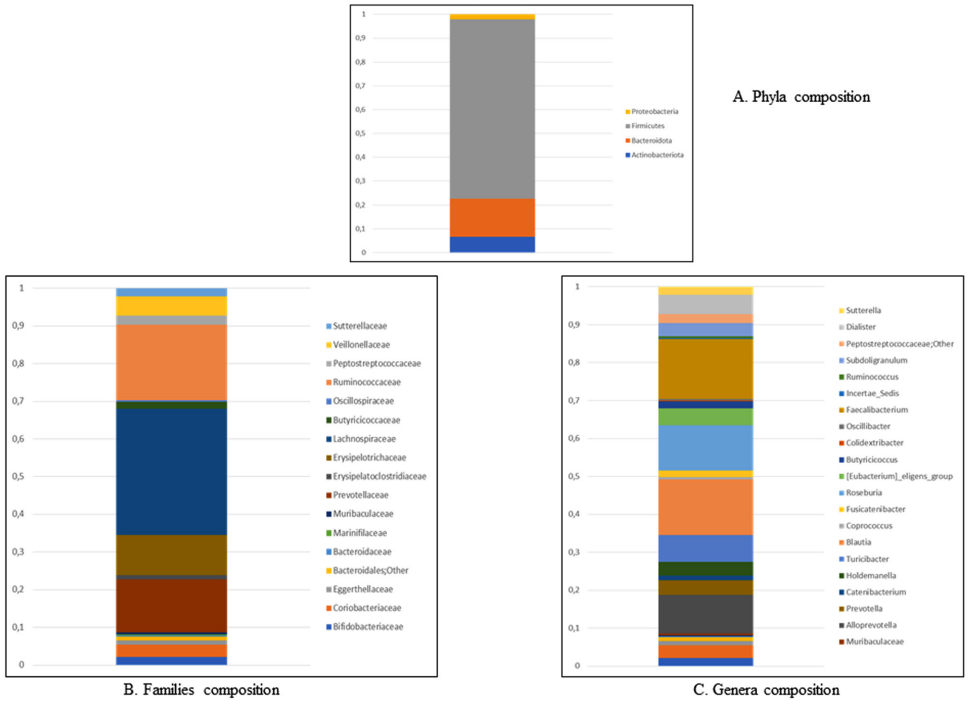


Fig. 1. (a) Gut microbiota in a SUDD patient without AD occurrence (case 1). (A) From the taxonomic point of view, the gut microbiota of this patient was characterized by the phyla Firmicutes and Bacteroidota, while the phyla Actinobacteriota and Proteobacteria were almost absent. (B) *Bacteroidaceae*, *Lachnospiraceae*, and *Ruminococcaceae* were the dominant families. As subdominant families, *Prevotellaceae*, *Peptostreptococcaceae*, and *Acidaminococcaceae* were the most represented. (C) Taxa belonging to *Lachnospiraceae* (primarily *Blautia* and *Roseburia*), *Ruminococcaceae* (*Faecalibacterium*), and *Bacteroidaceae* (*Bacteroides*) were the most represented genera, while *Prevotella* and *Phascolarctobacterium* were the most subdominant genera (the latter was absent in the gut microbiota of case 2). SUDD: symptomatic uncomplicated diverticular disease; AD: acute diverticulitis. (b) Gut microbiota in a SUDD patient with AD occurrence (case 2). (A) From the taxonomic point of view, the gut microbiota of this patient was characterized by the phyla Firmicutes and Bacteroidota. Differing for the microbiota of case 1, the phyla Actinobacteriota and Proteobacteria were largely represented as subdominant. (B) *Lachnospiraceae* and *Ruminococcaceae* were the dominant families, while *Bacteroidaceae* were very lowly expressed (in contrast to case 1). As subdominant families, *Prevotellaceae*, *Erysipelotrichaceae*, and *Veillonellaceae* were the most represented. (C) Taxa belonging to *Lachnospiraceae* (primarily *Blautia* and *Roseburia*), *Ruminococcaceae* (*Faecalibacterium*), and *Bacteroidaceae* (*Bacteroides*) were the most represented genera, while *Alloprevotella*, *Prevotella*, *Holdemanella*, *Turicibacter*, *Eubacterium eligens* group, and *Dialister* were the most subdominant genera, the majority of which were absent in the gut microbiota of case 1. SUDD: symptomatic uncomplicated diverticular disease; AD: acute diverticulitis.

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[11], were overrepresented, while *Phascolarctobacterium* and *Acidaminococcaceae* (the latter belonging to the *Clostridia* class and associated with significant response to therapy in ulcerative colitis [UC]) [11] were absent in comparison with the SUDD patient without AD occurrence. Finally, the abundance of the subdominant genera *Alloprevotella*, *Prevotella*, *Holdemanella*, *Turicibacter*, *Eubacterium eligens* group, and *Dialister* confirms that there is also a high heterogeneity of GM in AD following SUDD but with a higher number of genera linked to intestinal inflammation (*Prevotella* and *Alloprevotella*, *Turicibacter*, and *Dialister*).

While significant uncertainty remains, the data arising from these cases demonstrated that the GM shows mild changes in a SUDD patient without AD occurrence, while it shows more changes in a SUDD patient with AD occurrence during follow-up. Therefore, the GM may be one of the players involved in the occurrence of AD in SUDD, and further studies are warranted.

AUTHOR CONTRIBUTIONS

Antonio TURSI planned and conducted the study; Giorgia PROCACCIANTI, Federica D'AMICO, Rudi DE BASTIANI, and Silvia TURRONI collected data; Antonio TURSI, Giorgia PROCACCIANTI, Federica D'AMICO, Rudi DE BASTIANI, and Silvia TURRONI interpreted data; Antonio TURSI drafted the manuscript; and Antonio TURSI, Giorgia PROCACCIANTI, Federica D'AMICO, Rudi DE BASTIANI, and Silvia TURRONI approved the final draft submitted.

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CONFLICT OF INTEREST

Antonio TURSI served as a speaker and/or consultant for AbbVie, Bayer, Fenix Pharma, Galápagos, Janssen, Nalkein, Omega Pharma, and Sila. The remaining authors declare no competing interests.

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