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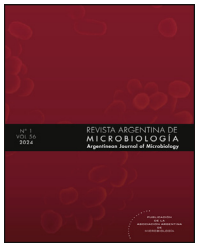

ORIGINAL ARTICLE

Dysgonomonas spp. in gastrointestinal pathology

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KEYWORDS
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Abstract *Dysgonomonas* spp. is a microorganism that is occasionally isolated in patients with gastroenteritis, although its clinical relevance remains uncertain. It has also been reported in association with other underlying conditions, especially in immunocompromised individuals. However, the exact role of *Dysgonomonas* spp. requires further investigation. Our objective was to link the pathogenesis of *Dysgonomonas* spp. with the clinical context in pediatric patients, evaluating its significance in gastroenteritis and related diseases. This was a retrospective and descriptive prevalence study involving the isolation of *Dysgonomonas* spp. from the fecal samples of pediatric patients presenting with digestive symptoms (from September 2019 to December 2023). The strains were isolated on a selective medium for *Campylobacter* spp., identified using the MALDI-TOF method, and their antibiotic sensitivity was assessed. Cases in which other gastrointestinal pathogens were isolated alongside *Dysgonomonas* spp. were excluded. Fifty cases of patients with *Dysgonomonas* spp. infection were analyzed, of which 45 (41 *D. capnocitophagoides*; four *D. gadei*) met the inclusion criteria. Among these, 77.8% were isolated episodes of gastroenteritis, whereas 22.2% were cases of persistent gastroenteritis (PG). Eighty percent (80%) of the cases occurred in the context of associated pathologies. All strains were sensitive to clindamycin and co-trimoxazole. In cases of alteration of the intestinal microbiota, usually related to specific underlying pathologies and other concomitant factors, *Dysgonomonas* spp. may act as an opportunistic pathogen.

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PALABRAS CLAVE
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Dysgonomonas spp. en patología gastrointestinal

Resumen *Dysgonomonas* spp. comprenden microorganismos ocasionalmente aislados de pacientes con gastroenteritis; el significado clínico de estos aislamientos es dudoso. Si bien se ha reportado su asociación con otras enfermedades, especialmente en individuos inmunocomprometidos, su papel aún no es claro. Nuestro objetivo fue relacionar la patogenia de *Dysgonomonas* spp. con su contexto clínico en pacientes pediátricos, evaluando su importancia en la gastroenteritis y enfermedades relacionadas. Se realizó un estudio retrospectivo y descriptivo que incluyó los aislamientos de *Dysgonomonas* spp. recuperados de muestras fecales de pacientes pediátricos con sintomatología digestiva asistidos en nuestro hospital, de septiembre de 2019 a diciembre de 2023. Las cepas se aislaron en medio selectivo para *Campylobacter* spp., se identificaron mediante MALDI-TOF y se estudió la sensibilidad antibiótica. Se registraron 50 casos de pacientes con infección por *Dysgonomonas* spp., de los cuales 45 (41 *Dysgonomonas capnocitophagoides*; 4 *Dysgonomonas gadei*) cumplieron los criterios de inclusión de este estudio. El 77,8% se presentaron como episodios aislados de gastroenteritis aguda y el 22,2% como gastroenteritis persistente; el 80% tuvo lugar en el contexto de patologías asociadas. Todas las cepas fueron sensibles a clindamicina y a cotrimoxazol. Se concluye que cuando hay alteración de la microbiota intestinal, habitualmente en relación con determinadas patologías de base y otros factores concomitantes, *Dysgonomonas* actuaría como patógeno oportunista.

Introduction

The genus *Dysgonomonas* contains four species: *D. capnocytophagoides*, *D. gadei*, *D. mossi*, and *D. hofstadii*[3,12]. These facultative anaerobic microorganisms, coccobacillus-shaped and Gram-negative-staining, could be part of the natural habitat of the intestinal tract[4], and only occasionally have been associated with bactereremia[1,2,5–7,10], abdominal[3,7,10–12], and gastrointestinal infections[4,9], mainly in patients with severe underlying diseases or immunocompromised conditions. Most cases involved *D. capnocytophagoides*, but *D. gadei*[3], *D. mossi*[8], and *D. hofstadii*[12] are also implicated. In gastrointestinal infections (diarrhea), the pathogenicity and clinical significance of this bacterium are unclear[12], and none of the few available reports are from pediatric patients.

In September 2019, the mass spectrometry method for bacterial identification (MALDI-TOF Biotyper, Bruker) was implemented in our laboratory, and since then, several strains of *Dysgonomonas* spp. have been isolated and identified in stool samples from pediatric patients.

The aim of this study was to assess the role of *Dysgonomonas* spp. in relation to episodes of diarrhea in pediatric patients seen at our hospital, and to confirm the usual antibiotic susceptibility pattern.

Methods

This observational retrospective study included all cases in which *Dysgonomonas* spp. were isolated from pediatric patients (under 18 years old) presenting with gastrointestinal symptoms (diarrhea) in our hospital (including those seen in the emergency department or admitted to hospital) from September 2019 to December 2023. The inclusion criteria required that *Dysgonomonas* spp. be the only microorganism isolated from the stool culture. Consequently, samples in which other gastrointestinal pathogens were isolated alongside *Dysgonomonas* spp. during the same clinical episode were not assessed. Two hundred and fifty fecal samples collected from pediatric patients without gastrointestinal symptoms who were admitted to our hospital were included as a control group.

The fecal samples from both the control group and the study group were analyzed using the current procedure for stool culture followed in our laboratory, which includes non-selective media (Columbia agar) and selective media for *Salmonella* spp. and *Shigella* spp. (SS agar), *Yersinia enterocolitica* (CIN agar), *E. coli* O157 (MacConkey-sorbitol agar), and *Campylobacter* spp. (Campylosel agar). All colonies morphologically compatible with gastrointestinal pathogens were identified using MALDI-TOF. When bacterial identification matched a gastrointestinal pathogen, antimicrobial susceptibility was assessed. All samples were also processed to detect rotavirus and adenovirus using an immunochromatographic method (Bioline Rota/Adeno. Abbott).

According to the clinical symptoms, some samples were also processed to detect *Clostridium difficile* by culture, enzyme immunoassay (C.Diff Quik Chek Complete. TechLab), and molecular methods (Xpert *C.difficile* BT. Cepheid), as well as parasites by direct microscopic examination. To complement the microbiological diagnosis, a molecular method was also used in specific cases (Filmarray GITM panel).

Clinical and analytical data were reviewed from the records of the included patients. When additional information was required, the physician in charge of each patient was consulted directly.

Table 1 Case distribution according to symptomatology, underlying pathology and treatment.

Pathology	Acute symptomatology				Persistent symptomatology			
	No underlying pathology	Treatment	Underlying pathology	Treatment	No underlying pathology	Treatment	Underlying pathology	Treatment
	6	0	29	4	3	3	7	2
Hematology-oncology patient			7					
Respiratory tract infection			6					
Intestinal milk and/or egg allergy							5	
Gastrointestinal motility disorders			4				2	
Heart surgery			3					
Pediatric inflammatory multisystem syndrome*			2					
Neurological surgery			1					
Altered intestinal absorption			1					
Systemic viral infection			1					
Leishmaniasis			1					
Intestinal inflammatory disease**			2					
Preterm with metabolic disease			1					
No underlying pathology	6				3			

* Pediatric inflammatory multisystem syndrome (PIMS; related to COVID-19).
** Intestinal inflammatory disease (Crohn's disease and/or ulcerative colitis).

Antimicrobial susceptibility was studied by the agar diffusion method on Mueller-Hinton agar + 5% defibrinated horse blood.

Results

From September 2019 to December 2023, a total of 8738 fecal samples were collected for stool culture analysis. Fifty cases of *Dysgonomonas* spp. were isolated from 50 patients, representing 0.57% of the samples analyzed, of which 45 (40 *Dysgonomonas capnocytophagoides*; 5 *Dysgonomonas gadei*) were identified by MALDI-TOF and matched the inclusion criteria. In five cases, other gastrointestinal pathogens were detected (three rotavirus, one *Clostridium difficile*, and one *Cryptosporidium* spp), which were not included in this study. Antimicrobial susceptibility tests showed that all strains were sensitive to clindamycin and co-trimoxazole and resistant to carbapenems. Tables 1 and 2 show the relationship among age, acute or persistent symptomatology, associated pathology, and treatment.

A single episode of acute gastrointestinal symptomatology was observed in 35 (77.8%) cases, while in the remaining 10 cases, the symptomatology was persistent and lasted several weeks or months. Regarding associated pathologies, in 36 (80%) cases, the patients presented with an underlying condition, including hematology-oncology disorders, respiratory tract infections, intestinal milk and/or egg allergy, or gastrointestinal motility disorders, among others. In contrast, in 10 (20%) cases, no other pathology was related. (Table 1).

The patients' age ranged from 14 days to 18 years (75.5% younger than three years), with 24 (53%) of them being female (Table 2).

Two hundred and fifty fecal samples collected from patients without gastroenteritis symptoms and submitted to calprotectin analysis were used as a control group. It is noteworthy that none of these samples showed the presence of *Dysgonomonas* spp.

In 18 cases (40%), all presenting with acute symptoms, previous antibiotic therapy was reported within the last two weeks.

In patients at higher risk, including those with underlying illnesses and important symptoms – mainly immunocompromised patients, as well as patients with persistent symptomatology, specific anti-*Dysgonomonas* antibiotic treatment was administered in nine cases (20%). Eight patients were treated with co-trimoxazole, and one with clindamycin. After the treatment, the gastrointestinal symptomatology (diarrhea) disappeared in four acute and two persistent cases. In the remaining three persistent cases, clinical symptoms decreased, but did not disappear completely.

After five or seven days of treatment and/or clinical recovery, a stool sample was cultured for a control follow-up

Table 2 Case distribution according to patient age and underlying pathology.

Pathology	≤1 month	>1 month–≤1 year	>1 year-≤3 years	>3 years–≤10 years	>10 years
	1 (2.2%)	15 (33.3%)	18 (40%)	5 (11.1%)	6 (13.3%)
Hematology-oncology patient			1	2	4
Respiratory tract infection		4	2		
Intestinal milk and/or egg allergy		1	4		
Gastrointestinal motility disorders		2	2	1	1
Heart surgery		3			
Pediatric inflammatory multisystem syndrome*			1	1	
Neurological surgery			1		
Altered intestinal absorption		1			
Systemic viral infection			1		
Leishmaniasis			1		
Intestinal inflammatory disease**				1	1
Preterm with metabolic disease	1				
No underlying pathology		4	5		

* Pediatric inflammatory multisystem syndrome (PIMS; related to COVID-19).
** Intestinal inflammatory disease (Crohn's disease and/or ulcerative colitis).

in 15 (33.3%) cases, and in none of them was *Dysgonomonas* spp. isolated again.

Discussion

The implementation of new methodologies, particularly MALDI-TOF mass spectrometry, has significantly improved the rapid and accurate identification of *Dysgonomonas* species in clinical samples. The ability to promptly identify these pathogens facilitates better clinical decision-making, especially in immunocompromised patients and those with persistent symptomatology. However, we cannot establish definitive conclusions regarding the pathogenicity of this microorganism in relation to gastrointestinal infection. This was due to the limited data available, mainly because, in most cases, the information recorded in the medical charts was sparse, and, follow-up after hospital discharge was not often possible. However, these findings suggest a specific pathogenic pattern: *Dysgonomonas* spp. (mainly *D. capnocytophagoides*) may act as an opportunistic pathogen in the case of probable microbiota disorders due to underlying illnesses or other concomitant factors, reinforcing the need for further investigation into its role in the pathogenesis of gastrointestinal diseases.

Overgrowth of this microorganism and replacement of microbiota may contribute to the development of clinical symptoms. In our patients, previous antibiotic therapy, allergic and inflammatory intestinal diseases, and disorders of intestinal motility were the most frequent underlying conditions. In hematology-oncology patients, immunosuppression is also an important factor. The pathogenic potential of *Dysgonomonas* spp. seems not to be outstanding, as all cases showed mild or moderate gastrointestinal symptomatology. None of them was severe, even when underlying illnesses were present. The recovery rate was possibly higher in the control group, suggesting that *Dysgonomonas* spp. may be responsible for these digestive manifestations.

Most cases occurred in patients younger than three years, probably due to predisposing factors such as digestive immaturity, which is more frequent at this age.

All isolated strains exhibited the same antibiotic susceptibility profile and matched former reports[1,3–7,9], which showed uniform sensitivity to clindamycin and cotrimoxazole, and variable results to carbapenems.

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Conflicts of interest

None declared.

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