

Campylobacteriosis: from diagnosis to the community intervention, a case-control study

Inês Silva-Costa^{1a*}, João Sousa-Marques^{1b}, Sara Geitoeira^{1c}, Catarina Dias^{2d}, Sara Dias^{3e},
Lígia M. Ferreira^{1f}, Sofia Reis^{1g}, and Cristina Baptista^{1h}

¹Serviço de Pediatria, Centro Hospitalar Tondela-Viseu E.P.E.; ²Serviço de Patologia Clínica, Centro Hospitalar Tondela-Viseu E.P.E.; ³Unidade de Saúde Pública, ACES Dão-Lafões. Viseu, Portugal

ORCID: ^a0000-0002-2940-838X; ^b0000-0002-2845-3357; ^c0000-0002-2298-1327; ^d0000-0002-8094-9827; ^e0009-0002-3494-1039; ^f0000-0003-1098-0420; ^g0009-0002-3667-9241; ^h0009-0002-8154-5920

Abstract

Introduction: Campylobacteriosis is the most frequent cause of acute bacterial diarrhea and its rising incidence in Europe is of concern. Guidelines for etiological investigation in acute infectious diarrhea and their impact on therapeutic conduct and community interventions are yet to be defined. **Materials and Methods:** We viewed 5 years of the Pediatric Emergency Department's stool cultures. The case group included 207 patients with Campylobacteriosis and the control group 276 patients with a negative stool culture. We evaluated the execution rate of Mandatory Notification and the diligence performed by Public Health Authorities. **Results:** In the case group, the median age was 2 years, 59.90% of patients were males and 68.60% were residents in rural areas. The bloody stool was significantly more frequent in the case group (78.26% vs. 30.80%, OR 8.09) and so was the presence of fever (65.22% vs. 39.86%, OR 2.83). In the case of group, 8.70% were admitted to in-patient facilities. The readmission rate in the subsequent 7 days was 17.87%, 45.95% of which with alterations to the previously chosen therapeutic conduct. The notification was performed in 37.63% of all Campylobacteriosis, translating most frequently isolated cases in the intervention area of the studied Health Authority. The most frequent diligence was sanitary education. In the group of patients whose notification was not performed, reinfection happened twice. **Conclusion:** Campylobacteriosis is in most cases a benign and self-limited disease. The isolation of the agent in the stool culture still plays a role in the management of the therapeutic conduct and the methods of community control.

Keywords: Campylobacteriosis. Diarrhea. Public Health.

Campilobacteriose: do diagnóstico à intervenção comunitária, um estudo de caso-controlo

Resumo

Introdução: A Campilobacteriose é a causa mais frequente de diarreia bacteriana aguda sendo preocupante a sua incidência crescente no espaço europeu. Estão ainda por definir orientações para a investigação etiológica na diarreia infecciosa aguda, o seu impacto no plano terapêutico e nas medidas interventivas na comunidade. **Materiais e Métodos:** Analisámos 5 anos de episódios de urgência com pedido de coprocultura anexo. Obteve-se uma população composta por um grupo caso de 207 culturas positivas para *Campylobacter* e um grupo controlo com 276 culturas negativas. Avaliámos o cumprimento da notificação obrigatória e as diligências efetuadas pela Saúde Pública. **Resultados:** A mediana de idades

*Correspondence:

Inês Silva-Costa
E-mail: c-ines@hotmail.com

Received: 30-03-2023
Accepted: 13-11-2023
<https://pjp.spp.pt>

Available online: 07-02-2024
Port J Pediatr. 2024;55(1):34-39
DOI: [10.24875/PJP.M23000133](https://doi.org/10.24875/PJP.M23000133)

2184-3333 / © 2023 Portuguese Society of Pediatrics. Published by Permayer. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

do grupo caso foi 2 anos. Destes, 59,90% eram do sexo masculino e 68,60% provenientes de um meio rural. A diarreia sanguinolenta foi significativamente mais frequente no grupo caso (78,26% vs. 30,80%, OR 8,09) assim como a presença de febre (65,22% vs. 39,86%, OR 2,83). No grupo caso optou-se por internamento em 8,70% dos doentes. A taxa de readmissões a 7 dias foi de 17,87%, 45,95% das quais com alterações do plano terapêutico. Notificaram-se 37,63% das Campilobacterioses, a maioria tratando-se de casos isolados na área de intervenção da Autoridade de Saúde Pública em estudo. A diligência mais comum foi a educação sanitária. No grupo de admissões não notificadas verificaram-se duas reinfeções. **Conclusão:** A Campilobacteriose é na maioria dos casos uma doença benigna e autolimitada e o seu isolamento em coprocultura continua a ter papel na gestão do plano terapêutico e dos métodos para controlo de focos na comunidade.

Palavras-chave: Campilobacteriose. Diarreia. Saúde Pública.

Keypoints

What is known

- Campylobacteriosis is the main cause of bacterial gastrointestinal infections worldwide.
- It usually presents as a self-limited, low morbimortality disease.
- It is a disease of mandatory notification to health authorities.

What is added

- Campylobacter was most frequently isolated in children with bloody diarrhea or fever.
- Notification to Public Health authorities is underperformed.
- Reinfection was more frequent in the group of patients whose notification was not performed.

Introduction

Acute diarrhea is one of the most frequent conditions that cause admission to pediatric emergency departments worldwide. In children without comorbidities and that don't present severity signs of illness, no etiologic investigation is usually required¹⁻².

Campylobacter is the main causative agent of acute bacterial diarrhea in medium-to-high-income countries. It usually presents as self-limited acute gastroenteritis in infants and adolescents. The treatment is mainly supportive and few cases require an antibiotic prescription. Epidemiological studies continue to identify changes in its seasonal pattern, with infections happening earlier than the previously stated summer season. On the other hand, the emergence of antimicrobial resistance is concerning and the incidence of campylobacteriosis is rising parallelly to the implementation of high hygiene and sanitary control standards that are required in European countries³⁻⁵.

Campylobacter is a commensal microorganism found in the gastrointestinal tracts of animals, including birds and cattle, and is prevalent in all avian species destined for human consumption. Water is another known source of contamination and European legislation mandates that natural mineral water sourced from springs and, occasionally, from drilling sources must be free from parasites and pathogens^{6,7}.

A well-structured surveillance program for campylobacteriosis is essential, as it provides vital information regarding the prevalence of the disease and helps

identify common routes of pathogen transmission. Therefore, it is crucial to implement standardized bio-control methods in the poultry sector and water supply. Patient notification is also of utmost importance as it enables public health authorities to trace the source of infection, thereby reducing community spread and the risk of reinfection⁶⁻⁸. Therefore, campylobacteriosis is a mandatory notification disease to Public Health departments that afterward conduct an epidemiological investigation and implement prevention and control measures. A correct and early notification allows more effective community interventions to prevent the short and long-term spread of the infection chain^{1,6,7}.

Our main purpose was to assess signs and symptoms more likely to be present in patients with campylobacteriosis, comparing to patients with acute infectious diarrhea from another bacteriological agent, and also gauge whether there were changes in the chosen therapeutic conduct after requesting the stool culture in the ED. Moreover, we intended to study the practical consequences of notifying the infection in preventing reinfection.

Methods

Study design and sample

A retrospective, case-control study was conducted in the pediatric emergency department (ED) of a level II hospital in Portugal, overviewing all patients who were admitted between the 1st of March 2015 and 31st of March 2020 and for whom a stool culture was requested

and analyzed at our Clinical Pathology Department. The patients were then assessed whether eligible for either case or control group. Stool cultures after April 2020 were excluded, as the COVID-19 pandemic started to spread in Portugal, and Public Health procedures were adapted to face this emergent pandemic.

The case group included all patients with isolation of a *Campylobacter* species in the stool culture performed through a selective agar base that incubates for up to 5 days in a microfilic environment at 42°C.

The control group included all patients without bacterial isolation in every stool culture performed (*Salmonella* and *Shigella* selective and differential agar, *Campylobacter* selective agar, *Yersinia* selective and differential agar, and the subculture performed in the gram-negative enriched agar). Exclusion criteria for the control group included: patients with inflammatory bowel disease or under immunosuppressive therapy, patients with positive polymerase chain reaction for adenovirus or rotavirus (PCR), or a final diagnosis that was not acute infectious diarrhea.

Data collection

Demographic and clinical variables were collected using the emergency admission records. The distinction between rural and urban areas was performed through the consultation of administrative records from Ministério da Administração Interna, namely “PRODER - Classificação das Freguesias do Continente em Rurais e Não Rurais”⁹. The therapeutic conduct was assessed through electronic medical prescriptions and discharge transcripts.

Notification of campylobacteriosis, epidemiological questionnaires, and the reports of the community interventions performed by Health Authorities were consulted in the archives of the local Public Health Department and Sistema Nacional de Vigilância Epidemiológica (SINAVE®) system.

Data analysis

Statistical Package for Social Sciences (SPSS®) version 26 software was used to analyze the collected data. The quantitative variables were expressed as central tendency measures and the qualitative variables as absolute values and percentages. Given the non-normal distribution of continuous variables, non-parametric tests were used. Values for $p < 0.05$ were considered statistically significant.

Approval by the Ethics Committee of the Hospital and the Public Health Department was obtained before initiating data collection.

Table 1. Qualitative variables

Variable	Control group (n = 276) n (%)	Case group (n = 207) n (%)	p value*
Sex (males)	160 (57.97)	124 (59.90)	0.64
Residence (rural area)	169 (61.23)	142 (68.60)	0.09
Vomiting	113 (40.94)	58 (28.02)	< 0.01
Fever	110 (39.86)	135 (65.22)	< 0.01
Abdominal pain	90 (32.61)	69 (33.33)	0.92
Bloody stool	85 (30.80)	162 (78.26)	< 0.01
Epidemiological context	70 (25.36) [‡]	42 (20.29) [†]	0.19
Admission to ED < 15 days	72 (26.09)	55 (26.57)	0.19

*Chi-Squared test.

[†]76 missing data.

[‡]99 missing data.

Results

During the five-year study period, 1089 stool cultures were requested in the ED. *Campylobacter* was isolated in the culture of 209 patients, two of whom were excluded from the case group due to missing clinical data.

Of the remaining 880 patients, 521 were eligible for the control group. The group of 359 patients not eligible included patients to whom only a certain type of bacteriological subculture was performed and, more infrequently, patients with isolation of another bacteriological agent rather than *Campylobacter*.

Exclusion criteria were then applied, with five patients excluded due to previous history of inflammatory bowel disease or recent immunosuppressive therapy and 240 without a final diagnosis of acute infectious diarrhea, leaving 276 patients to be included in the final control group.

Clinical presentation

The case and control groups were similar in age, sex, and area of residence (Tables 1 and 2).

Vomiting was the only clinical feature significantly more frequent in the control group. On the other hand, fever and bloody stool were more common in the case group, with an odds ratio of 2.83 (IC95% [1.95;4.11]) and 8.09 (IC95% [6.71;10.75]), respectively.

The median number of reported stools per day was significantly different in the extreme age groups, both higher in patients with campylobacteriosis (Table 3).

Table 2. Quantitative variables

Variable	Control group (n = 276) Median (variance)	Case group (n = 207) Median (variance)	p value*
Age in years	2.00 (20.18)	2.00 (12.18)	0.37
Illness evolution in days	4.00 (138.05)	3.00 (72.01)	< 0.01
Number of stools per day	5.00 (8.48)	6.00 (12.93)	< 0.01

*Mann Whitney U for independent samples.

Table 3. Median number of stools per day, per age group

Age group	Median number of stools per day (variance)		p value*
	Control group (n = 215) [†]	Case group (n = 165) [‡]	
≤ 1 year	4.00 (6.02)	6.00 (9.98)	0.02
(1-2) years	5.00 (11.20)	6.00 (10.20)	0.09
(2-4) years	6.00 (5.78)	6.00 (26.05)	0.51
> 4 years	4.00 (9.54)	6.00 (14.34)	0.01

*Mann-Whitney U test for independent samples.

[†]61 missing data.[‡]42 missing data.

From the case group, 18 (8.70%) were admitted to in-patient facilities, in contrast with 39 (14.13%) in the control group. The main reason for in-patient admission was suspected bacteremia and dehydration/electrolytic alterations. Regarding antibiotic treatment, only ceftriaxone was an empirically chosen therapeutic conduct in patients at admission, 4 (22.2%) in the case group and none in the control group.

In the case group, after telephonic contact with caregivers or through readmission in the ED, an antibiotic was prescribed in 34 (16.40%) patients, most frequently azithromycin (52.94%), all because of persistent symptoms.

Recorded readmissions to the ED, due to persistence or recrudescence of symptoms, in the seven subsequent days, were 17.87% in case group and 10.87% in the control group. Readmissions in the control group resulted in the change of management plan in two patients, who collected new stool cultures, both negative. On the other hand, readmissions in the case group resulted in the change of plan 45.95% of the time, most frequently initiating antibiotics.

Community intervention

From the total amount of patients diagnosed with Campylobacteriosis, 186 (89.86%) were residents in the area covered by the local Public Health Authority. Mandatory Notification was performed in 70 cases (37.63%), with a median time between diagnosis and notification of 6 days and a median time between the beginning of symptoms and notification of 13 days.

After epidemiological questionnaires were analyzed, three clusters were confirmed, two of them in family settings and one involving 9 children through contaminated water.

Sanitary education, such as food hygiene and safety procedures, personal hygienic care measures, and veterinary advice, if contact with animals was found as a possible contamination source, was the most frequent diligence, performed by Health Authorities, in 100% of identified cases. Water sample analysis was required in 28 cases: 19 private water sources, six public water fountains, one kindergarten, one private pool, and one water spring. Of the seven public water sources tested (water fountains and water springs), six were considered positive.

There were no reinfections registered in the group of patients who were notified. Furthermore, two patients were reinfected in the group whose notification was not performed, with a time gap of 4 and 10 months each. In our geographical area, for the pediatric population, if 58 notifications are performed, one case of reinfection is prevented.

Discussion

Campylobacteriosis is still a benign and self-limited disease in most cases. In our study, the mean age of diagnosis is compatible with the literature's description of higher prevalence in preschoolers^{2,3}. Bloody stool and fever may be associated with the isolation of *Campylobacter* in the stool cultures, with the first showing a stronger association. Vomiting is the only clinical feature associated with no isolation, which may be because, according to the literature, it is clinically more present when viral agents are involved.

Stool cultures continue to play an important role in the management of acute campylobacteriosis, with a non-neglectable proportion of children requiring antibiotic treatment. A positive stool culture, when children are readmitted for the persistence of symptoms, may lead to more antibiotic prescriptions, although it is not certain if this therapeutic conduct actually changes the natural progression of the disease¹.

Rural areas were not associated with a higher incidence of campylobacteriosis. The same was found in the epidemiological context. The latter needs careful evaluation as the control group might include children infected with viral agents, which also spread frequently in the pediatric population. However, in the case group, the epidemiological context should indicate that cohabitants would more likely be also infected with *Campylobacter*, and that was not found in the data extracted from the public health authorities, as just three outbreaks were confirmed. This might be a limitation of low rates of notification.

Notification to Public Health Authorities is still underperformed in our center, with more than half of the affected individuals without the potential care of public health authorities. However, in every patient whose notification was performed, an investigation was conducted by Health Authorities, which translates into full rates of management if proper reporting by pediatricians is performed. In the group of patients whose infection was notified, the time gap between the beginning of symptoms and the notification date, 13 days, is of note. This may pose difficulties in the management of the infection chain as it delays the investigation of possible contaminated sources that may have been discarded in that period, namely contaminated food. On the other hand, *Campylobacter* species is thermotolerant and grows at pH between 6.5 and 7.5, which are conditions difficult to maintain stable in natural environments exposed to changes in temperature, humidity, and acidity, increasing the potential of false negative sampling after several days of exposure^{6,7}. However, the efficacy of water sampling in our population was very high in public sources, as 6 out of 7 were positive. This should raise awareness of two problems: freshwater consumption implies that no heating is performed to eliminate coliforms and therefore individuals who drink it are more susceptible to infection compared to food that undergoes cooking, and, on the other hand, public water sources should be the ones with higher water quality, compared to private water sources that, by legislation, are not required to undergo frequent testing^{6,10}.

Reinfection rate in the children whose notification was not performed, with a large period of interval time, showing that although a benign course of infection happened, continuous exposure to the agent is still a risk factor for reinfection. Public health diligence should focus on stopping the primary source to prevent this from happening as more infections and reinfections translate into more bacterial gastroenteritis, more school or work absence, more admission to the

emergency departments, and higher rates of Guillain-Barré Syndrome and Reactive Arthritis, which are both known complications of campylobacteriosis⁶. The impact of campylobacteriosis on the overall public health burden of acute gastrointestinal illness remains uncertain. Numerous studies conducted have aimed to calculate the expenses associated with gastrointestinal infections, including campylobacteriosis. In a Swiss study, researchers determined that the average cost of a laboratory-confirmed case of Campylobacteriosis is approximately 975 euros¹¹. Therefore, accounting for the number of infected people in our center, the prevention of this infectious disease also translates into a cost-efficient activity as zoonotic diseases are more easily preventable compared to other environmental exposure lead pathologies. The costs associated with undiagnosed cases tend to vary more widely, with most studies focusing on underdiagnosis rather than underreporting.

This study assesses only the pediatric population, and this may pose a bias in the study of community interventions since we do not assess whether adults were also infected/reinfected in the families of children whose notification was not performed. There is still a big group of children, whose area of residence was not the one where the hospital was located, and because of that, we may have lost them for follow-up of readmission to the ED, notification to the public health department, and reinfection.

In conclusion, although campylobacteriosis is mostly a benign infection, it is also a preventable one. Notification to Public Health Authorities should be performed as reinfection is a reality and all cases are readily evaluated after correct reporting, with a considerable rate of potential-changing lead findings. The decrease in incidence may happen after correct notification of every case and if there is a shorter period between the beginning of symptoms and the public health investigation.

Acknowledgments

The results of this investigation were presented in 1^{as} Jornadas Digitais de Pediatria, on the 29th of October 2020.

Funding

None.

Conflicts of interest

None.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

References

- Rodrigues F, Calvino J, Alves AF, Lemos L. Diarreia Aguda por *Campylobacter* Jejuni. 2006. *Acta Med Port*; (3), Vol 37. 91-3.
- Soares AT, Couto C, Romão P, Melo IS, Braga M, Diogo J, et al. Gastroenterite Aguda por *Campylobacter* Spp: Casuística de uma Urgência Pediátrica [Acute gastroenteritis by *Campylobacter* spp: a retrospective study of a paediatric emergency department]. *Acta Med Port*. 2014 Sep-Oct;27(5):556-60.
- Borges AC, Pedrosa C, Santos A, Vitorino M, Costa M, Godinho C. *Campylobacter* jejuni: Gastroenterites Agudas e Infecções Extra-Intestinais. *Acta Med Port*; 2005;36(4):191-3.
- Patrick ME, Henao OL, Robinson T, Geissler AL, Cronquist A, Hanna S, et al. Features of illnesses caused by five species of *Campylobacter*, Foodborne Diseases Active Surveillance Network (FoodNet) - 2010-2015. *Epidemiol Infect*. 2018 Jan;146(1):1-10.
- Fitzgerald C, Patrick M, Gonzalez A, Akin J, Polage CR, Wymore K, et al. Multicenter evaluation of clinical diagnostic methods for detection and isolation of *Campylobacter* spp. from the stool. *J Clin Microbiol*. 2016;54(5):p. 1209-15.
- Facciola A, Riso R, Avventuroso E, Visalli G, Delia SA, Lagana P. *Campylobacter*: from microbiology to prevention. *J Prev Med Hyg*. 2017;58(2):E79-E92.
- The Institute of Environmental Science and Research Ltd. Notifiable Diseases in New Zealand: Annual Report 2016.
- Hlshwayo DF, Sigauque B, Noormahomed EV, Afonso SMS, Mandomando IM, Bila CG. A systematic review and meta-analysis reveal that *Campylobacter* spp. and antibiotic resistance are widespread in humans in sub-Saharan Africa. *PLoS One*. 2021 Jan 27;16(1):e0245951.
- Ministério da Agricultura e do Mar. PRODER - Classificação das Freguesias do Continente em Rurais e Não Rurais. 2020.
- Bull SA, Allen VM, Domingue G, Jorgensen JA, Frost R, Ure R, et al. Sources of *Campylobacter* spp. colonizing housed broiler flocks during rearing. *Appl Environ Microbiol*. 2006;72:645-52.
- Schmutz C, Mausezahl D, Bless PJ, Hatz C, Schweglen M, Urbinello D. Estimating healthcare costs of acute gastroenteritis and human campylobacteriosis in Switzerland. *Epidemiol Infect*. 2017;145(4):627-41.