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Original Research Article

The Impact of Gastrointestinal PCR on the Management of Gastrointestinal Infections in Immunocompromised Patients

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Abstract

Introduction*:** Gastrointestinal infections are one of the leading causes of morbidity and mortality throughout the world, particularly in the immunocompromised. Gastrointestinal PCR appears to be the technique of choice for establishing the molecular diagnosis of pathogenic gastrointestinal agents. The aim of this study was to establish the epidemiological, clinical and evolutionary profile of gastrointestinal infections and to study the impact of molecular diagnosis on the choice of a targeted therapy. ***Methods: This is a retrospective study carried out in the Microbiology Department of Arrazi Hospital of the Mohamed VI University Hospital Center, including all immunocompromised patients treated for a gastrointestinal infection and needing a hospitalization in the various departments, over a period of 15 months. ***Results*:** During the period studied, 124 patients were collected. The average age of the patients was 22 years. Signs of gastrointestinal infection were present in all patients. Of the patients sampled, 95.2% received probabilistic antibiotic therapy. Gastrointestinal infection has been documented in 57.26% of patients. A bacterial etiology was found in 76.81% of patients. A viral etiology was found in 13.04% of the patients and a parasitic etiology was found in 10.15% of the patients. Enteropathogenic E. coli was the most common infectious agent detected (19.53%). Co-infections were found in 29.84% of patients. Following PCR results, management was changed in 70 patients (56.45%), including initiation or modification of antibiotics in 40 patients (32.26%) and discontinuation of antibiotic therapy in 30 patients (24.19%). ***Conclusion*:** The diagnosis of gastrointestinal infections by multiplex PCR allowed us to provide optimal patient care with a reduction in the unnecessary use of antibiotics and an improvement in the course of care.

Keywords: Antibiotic therapy - Molecular diagnosis - Immunocompromised - Gastrointestinal infections - Impact of PCR.

INTRODUCTION

Gastrointestinal infections are a leading cause of morbidity and mortality worldwide. They represent a major public health issue given their prevalence and severity, particularly in immunocompromised patients. In developing countries, the World Health Organization (WHO) estimates that 3 to 3.2 million children die each year from the consequences of gastroenteritis (Gallay A *et al.*, 2003) (Huilan S *et al.*, 1991). Until the 1970s, diagnostic techniques for infectious diarrhea only made it possible to identify the etiological agent for a small proportion of cases of gastrointestinal infections (bacteria, protozoa). Since the 1990s, molecular biology methods have enabled the identification of an increasing number of viruses and have shown in particular that more than two thirds of epidemics of gastrointestinal infections are of viral origin (Gallay A *et al.*, 2003) (Dedman D *et al.*, 1998).

The use of diagnosis by syndromic approach by the gastrointestinal PCR panel makes it possible to have precise microbiological documentation, with simultaneous research of the 22 most frequently incriminated pathogens and to have a result in just a few hours, from a single stool sample (Vinjé J *et al.*, 1996). Patient care will then be rapid and effective because it will be adapted to the isolated pathogen, while limiting the inappropriate use of antibiotics.

The aim of this study was to draw up the epidemiological, clinical and evolutionary profile of

gastrointestinal infections, to establish the etiological diagnosis and to study the impact of molecular diagnosis on the choice of a targeted therapy.

MATERIAL AND METHODS

Type and framework of the study: This is a retrospective cross-sectional study carried out within the Microbiology department of the Arrazi hospital of the CHU Mohamed VI, including all immunocompromised patients treated for a gastrointestinal infection and which required hospitalization in the various departments within the Arrazi hospital of the CHU Mohamed VI in Marrakech.

Duration of the study: This work was carried out over a period of 15 months, from October 2018 to December 2019.

Inclusion criteria: All immunocompromised patients hospitalized in the various departments within the Arrazi Hospital of the CHU Mohamed VI, who underwent gastrointestinal PCR during the study period, were included in this study.

Exclusion criteria: Were excluded:

- Immunocompetent patients.
- Patients who have not undergone gastrointestinal PCR.
- Patients treated on an outpatient basis without a medical file.

Data collection: Data collection was done from the database of the microbiology department and the hospitalization records of patients admitted to the various departments of the Arrazi Hospital of the CHU Mohamed VI in Marrakech.

Data analysis: We used Microsoft Excel 2016 software for statistical data analysis. These were converted to percentage, mean or median.

The gastrointestinal filmarray panel: it is a simple and firm system, which involves the processing, amplification, identification and analysis of samples, allowing results to be obtained in approximately one hour, with only 2 minutes preparation time. The targets of the panel include thirteen bacteria (enteroaggregative E. coli (EAEC), enterotoxigenic E. coli (ETEC), enteropathogenic E. coli (EPEC), shiga toxin-producing E. coli (STEC), E. coli O157, Enteroinvasive E. coli (EIEC) / Shigella spp, Campylobacter (jejuni / coli / upsaliensis), Vibrio (parahaemolyticus / vulnificus), Salmonella spp, Plesiomonas shigelloides, Yersinia enterocolitica, Clostridium difficile (toxin A / B), and Vibrio cholera), five viruses (Adenovirus F40/41, Astrovirus, Norovirus GI/GII, Rotavirus A, and Saprovirus (I, II, IV, V)) and four parasites (Cryptosporidium spp, Giardia lamblia, Cyclospora Cayetanensis, and Entamoeba histolytica)

Ethical Approval: Informed verbal consent from patients was obtained prior to enrolling them in the study. No ethical approval was sought for the analysis of the dataset as it does not contain any personally identifiable information.

RESULTS

Epidemiological characteristics of patients: 124 hospitalized patients were included in this study. These patients ranged in age from 2 months to 93 years, with a median age of 22 years. Of the 124 patients, 67 were male (54.03%) and 57 were female (45.97%), with a sex ratio M/F of 1.18.

Distribution of patients in hospital departments: During this period, 23.48% of patients were hospitalized in the Infectious Diseases department, 18.55% in Pediatrics B, 16.22% in the Hematology, 9.78% at the level of the Gastrology department, 6.55% at the level of Pediatric intensive care, 6.55% at the level of Pediatrics A, 5.75% at the level of the Nephrology department, 4.85% at the level of Medical Resuscitation, 2.52% at the level of the Rheumatology department, 1.63% at the level of Pediatric Emergencies, 0.8% at the level of the Neurology department and 0.8% at the level of the Surgery department visceral.

The immune profile of the patients: Concerning the immune profile of the patients, 30% of the patients had a retroviral infection and 5.6% had AML. Table 1 summarizes the defects and the immune status of the patients.

Probabilistic antibiotic therapy

This study showed that 95.16% of patients received probabilistic antibiotic therapy. Several molecules were administered, with a predominance of 3rd generation cephalosporins in 27.42% of patients, followed by Ciprofloxacin in 12% of patients (Figure 1).

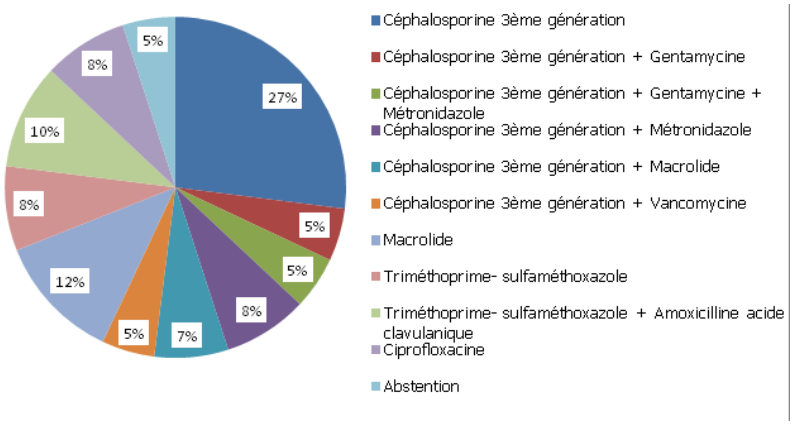

Figure 1: Répartition des différentes molécules administrées en antibiothérapie probabiliste.

Results of gastrointestinal PCR

Among all the patients sampled during this period, gastrointestinal infection was documented in 71 patients, i.e. an overall positivity rate of 57.26%. Co-infections were found in 37 patients, i.e. 52.11%.

The set of germs identified was 128 germs. Enteropathogenic E.coli was the most detected infectious agent (n=25), followed by Enteroaggregative E.coli (n=21), Campylobacter (n=12) and Cryptosporidium (n=10). The distribution of identified pathogens is shown in Figure 2.

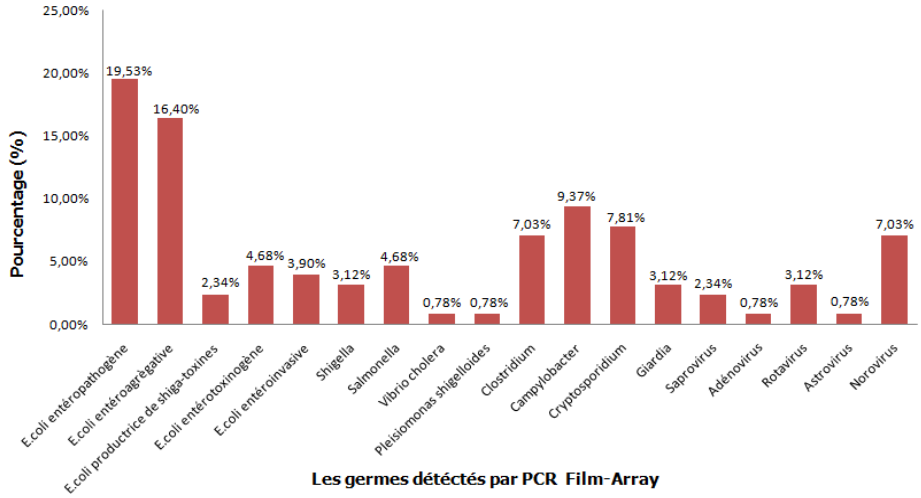

Figure 2: Répartition des différents agents pathogènes détectés par PCR (n=128)

Within these detected gastrointestinal infections (n=71), a bacterial etiology was found in 76.81% of patients either in mono or co-infection. A viral etiology was found in 13.04% of patients, and a parasitic etiology was found in 10.15% of patients.

The proportion of each pathogen identified in the co-infection was different between the agents studied. Table 2 shows the proportion of pathogens detected in mono and co-infection. The most found association was Campylobacter and Cryptosporidium co-infection in 12.8% of cases.

Treatment after PCR results:

- Antibiotic therapy was stopped in 1.6% of patients who had an isolated viral etiology (not associated with other pathogens). Antibiotic therapy was also stopped in patients with E. coli producing shiga-toxins and which present 7.25% of patients. During the clinical suspicion of gastrointestinal infection of bacterial origin not confirmed after the PCR, the treatment initiated by the antibiotics was stopped in 14.5% of the patients. So in total antibiotic therapy was stopped in 23% of patients after the PCR results.
- 76.58% of patients were treated with antibiotic therapy. It was maintained in 28.23% of patients in whom bacterial GI infection was suspected with a negative PCR result. Initial antibiotic therapy was maintained in 16.13% of patients. Antibiotic therapy was modified in 27.42% of patients and initiated in 4.8%.

DISCUSSION

In the present study, gastrointestinal infection was microbiologically documented in 71 patients, an overall positivity rate of 57.26%. Similar studies conducted in the United States and Italy have presented

an approximate positivity rate (Rintala A *et al.*,) (Calderaro A *et al.*,).

The distribution of pathogens over this period showed the predominance of bacterial etiology, which has also been reported in several studies (Yang Y *et al.*,) (Ramakrishnan B *et al.*,) (Christian Leli *et al.*,).

Enteropathogenic E.coli was the most found bacterial agent in our series, which is consistent with other similar studies. (Axelrad JE *et al.*,) (Becker SL *et al.*,). Christian Leli et al found the predominance of salmonella, in a study on the evaluation of the multiplex gastrointestinal PCR panel for the etiological diagnosis of infectious diarrhea. (Christian Leli *et al.*,). In the present study, the most found virus was Norovirus. The predominance of Norovirus has also been reported by several studies. (Huang SH *et al.*,) (Ramakrishnan B *et al.*,). Cryptosporidium presented the predominant parasitic agent in our series.

Thus, the important role of co-infections in gastrointestinal infections in immunocompromised patients has been widely reported by several studies. (Huang SH *et al.*,) (Frickmann H *et al.*,). This study reports a coinfection percentage of 52.1%.

During gastrointestinal infections, empirical treatment with antibiotics is frequently prescribed, although the etiology of these infections may be bacterial, viral or parasitic. Thus, the prescription of antibiotics is not always indicated and has harmful consequences, particularly on the emergence of bacterial resistance to antibiotics. Hence the interest of this syndromic approach, thanks to its good specificity and sensitivity, and its high detection capacity, the FilmArray Platform is presented as a technique of choice to limit this abusive prescription of antibiotics and allow better control of the infectious risk.

A study conducted in New York by Axelrad et al showed that patients who received gastrointestinal PCR were 11% less likely to receive antibiotic therapy, compared to patients tested by conventional stool culture. The notable reduction in antibiotic prescribing for patients who received PCR-based testing means that gastrointestinal PCR panels could be a useful tool to promote antibiotic stewardship. Axelrad et al note that antibiotics were still used in about a third of patients (Axelrad JE *et al.*,).

A study conducted in Arizona in 2017 showed that the implementation of the FilmArray gastrointestinal panel provided several benefits in the management of antibiotics, including: higher diagnostic yield, faster results, higher rates of discontinuation antibiotics, shorter time for antibiotic adjustment and lower rate of inappropriate antibiotic (Beatty N *et al.*,).

In America, a study by Stacy G Beal et al showed that the GI panel improved patient care by rapidly identifying a wide range of pathogens that might otherwise have gone undetected, reducing the need for other diagnostic tests, reducing unnecessary use of antibiotics and leading to a reduction in length of hospital stay. (Beal SG *et al.*,).

Another study conducted in America in 2016 showed that the management of 78% of patients was modified after the results of the FilmArray gastrointestinal panel test including the initiation or modification of antibiotics in 50% of patients and discontinuation of antibiotic therapy in 28% of patients (Kati Shihadeh *et al.*,). A study conducted in Washington between July 2015 and December 2016 showed that after the introduction of the FilmArray gastrointestinal panel test, the time to initiate optimal antibiotics was shorter (Torres-Miranda D *et al.*,).

Results interpretation limits

This study has limitations that are worth discussing:

- As this was a retrospective study, we had no control over the choice of conventional investigations ordered by the attending physician.
- Second, detection of multiple pathogens may reflect active co-infection, or remote infection.
- Not all microorganisms detected by PCR correspond to infections. PCR can detect asymptomatic carriers.
- Although we have shown that multiplex PCR allows faster diagnosis and better management of the disease, the economic impact of this test on public health has not been assessed.
- Given our data collection methods and sample size, the results may not be generalizable to the entire population. Nevertheless, the reported results could be targets for future studies.

CONCLUSION

In conclusion, molecular biology techniques are promising techniques that offer better sensitivity and specificity and considerable time savings compared to conventional diagnostic methods. These techniques have enabled us to determine the epidemiological profile of gastrointestinal infections and to confirm their etiologies, particularly in immunocompromised patients. The FilmArray Multiplex PCR Panel detects a wide range of gastrointestinal pathogens, including viruses and co-infections. The diagnosis of gastrointestinal infections by PCR is a simple and rapid test with high sensitivities and fast turnaround times. Thus, it may help to reduce empiric antibiotic treatment and may be a valuable tool for early initiation and monitoring of antibiotic therapy. The economic impact of multiplex PCR was not evaluated in our study. Further studies should be carried out in this direction.

Conflicts of interest: The authors declare no conflict of interest.

RÉFÉRENCES

- Gallay, A., Vaillant, V., De Valk, H., & Desenclos, J. C. (2003). Epidémiologie des diarrhées. Encycl. Med. Chir. (Elsevier AS, Paris) Gastro-entérologie, 9-001-B, 7P.
- Huilan, S., Zhen, L. G., Mathan, M. M., Mathew, M. M., Olarte, J., Espejo, R., ... & Sami, Z. (1991). Etiology of acute diarrhoea among children in developing countries: a multicentre study in five countries. *Bulletin of the World Health Organization*, *69*(5), 549-555.
- Dedman, D., Laurichesse, H., Caul, E. O., & Wall, P. G. (1998). Surveillance of small round structured virus (SRSV) infection in England and Wales, 1990–5. *Epidemiology & Infection*, *121*(1), 139-149.
- Vinje, J., & Koopmans, M. P. (1996). Molecular detection and epidemiology of small round-structured viruses in outbreaks of gastroenteritis in the Netherlands. *Journal of Infectious Diseases*, *174*(3), 610-615.
- Rintala, A., Munukka, E., Weintraub, A., Ullberg, M., & Eerola, E. (2016). Evaluation of a multiplex real-time PCR kit Amplidiag® Bacterial GE in the detection of bacterial pathogens from stool samples. *Journal of microbiological methods*, *128*, 61-65.
- Calderaro, A., Martinelli, M., Buttrini, M., Montecchini, S., Covan, S., Rossi, S., ... & De Conto, F. (2018). Contribution of the FilmArray® Gastrointestinal Panel in the laboratory diagnosis of gastroenteritis in a cohort of children: a two-year prospective study. *International Journal of Medical Microbiology*, *308*(5), 514-521.
- Yang, Y., Rajendran, V., Jayaraman, V., Wang, T., Bei, K., Krishna, K., ... & Krishnamurthy, H. (2019). Evaluation of the Vibrant DNA microarray for the high-throughput multiplex detection of enteric pathogens in clinical samples. *Gut pathogens*, *11*(1), 1-12.
- Ramakrishnan, B., Gopalakrishnan, R., Senthur Nambi, P., Durairajan, S. K., Madhumitha, R., Tarigopula, A., ... & Ramasubramanian, V. (2018). Utility of multiplex polymerase chain reaction (PCR) in diarrhea—An Indian perspective. *Indian Journal of Gastroenterology*, *37*(5), 402-409.
- Leli, C., Di Matteo, L., Gotta, F., Vay, D., Cavallo, V., Mazzeo, R., ... & Rocchetti, A. (2020). Evaluation of a multiplex gastrointestinal PCR panel for the aetiological diagnosis of infectious diarrhoea. *Infectious Diseases*, *52*(2), 114-120.
- Axelrad, J. E., Joelson, A., Nobel, Y., Whittier, S., Lawlor, G., Riddle, M. S., ... & Lebwohl, B. (2018). The distribution of enteric infections utilizing stool microbial polymerase chain reaction testing in clinical practice. *Digestive Diseases and Sciences*, *63*(7), 1900-1909.
- Becker, S. L., Chatigre, J. K., Gohou, J. P., Coulibaly, J. T., Leuppi, R., Polman, K., ... & von Müller, L. (2015). Combined stool-based multiplex PCR and microscopy for enhanced pathogen detection in patients with persistent diarrhoea and asymptomatic controls from Côte d'Ivoire. *Clinical microbiology and infection*, *21*(6), 591-e1.
- Huang, S. H., Lin, Y. F., Tsai, M. H., Yang, S., Liao, M. L., Chao, S. W., & Hwang, C. C. (2018). Detection of common diarrhea-causing pathogens in Northern Taiwan by multiplex polymerase chain reaction. *Medicine*, *97*(23), e11006.
- Ramakrishnan, B., Gopalakrishnan, R., Senthur Nambi, P., Durairajan, S. K., Madhumitha, R., Tarigopula, A., ... & Ramasubramanian, V. (2018). Utility of multiplex polymerase chain reaction (PCR) in diarrhea—An Indian perspective. *Indian Journal of Gastroenterology*, *37*(5), 402-409.
- Frickmann, H., Schwarz, N. G., Rakotozandrindrainy, R., May, J., & Hagen, R. M. (2015). PCR for enteric pathogens in high-prevalence settings. What does a positive signal tell us?. *Infectious Diseases*, *47*(7), 491-498.
- Axelrad, J. E., Freedberg, D. E., Whittier, S., Greendyke, W., Lebwohl, B., & Green, D. A. (2019). Impact of gastrointestinal panel implementation on health care utilization and outcomes. *Journal of clinical microbiology*, *57*(3), e01775-18.
- Beatty, N., Nix, D., August, J., Swazo, R., Mckeown, K., Alshibani, M., ... & Al Mohajer, M. (2017). Rapid multiplex gastrointestinal pathogen panel testing improves antibiotic stewardship in patients with suspected infectious diarrhea compared with conventional methods. In *Open Forum Infectious Diseases* (Vol. 4, No. Suppl 1, p. S624). Oxford University Press.
- Beal, S. G., Tremblay, E. E., Toffel, S., Velez, L., & Rand, K. H. (2018). A gastrointestinal PCR panel improves clinical management and lowers health care costs. *Journal of clinical microbiology*, *56*(1), e01457-17.
- Shihadeh, K., Young, H., Knepper, B., & Jenkins, T. (2016, December). Impact of a Stool Multiplex Polymerase Chain Reaction Rapid Diagnostic Test on Antibiotic Prescribing in Patients Hospitalized With Diarrhea of Suspected Infectious Etiology. In *Open Forum Infectious Diseases* (Vol. 3, No. suppl_1, p. 213). Oxford University Press.
- Torres-Miranda, D., Akselrod, H., Karsner, R., Secco, A., Silva-Cantillo, D., Siegel, M. O., ... & Simon, G. L. (2020). Use of BioFire FilmArray gastrointestinal PCR panel associated with reductions in antibiotic use, time to optimal antibiotics, and length of stay. *BMC gastroenterology*, *20*(1), 1-7.