ADITUM
Enrich your Research

Clinical Medical Case Reports and Case Series

Research Article

Comparison of Methods for Diagnosis of Gastrointestinal Diseases

Isabelle Basbouss-Serhal[1*], Fatima Fayad[2]
Head of pathology and molecular laboratory Siblin Governmental Hospital, Lebanon

Article Info

Received: January 03, 2025
Accepted: January 06, 2025
Published: January 10, 2025

***Corresponding author:** Isabelle Basbouss-Serhal, Head of pathology and molecular laboratory Siblin Governmental Hospital, Lebanon.

Citation: Isabelle Basbouss-Serhal. (2025) "Comparison of Methods for Diagnosis of Gastrointestinal Diseases.", Clinical Medical Case Reports and Case Series, 2(1); DOI: 10.61148/3065-7644/CMCRCS/16

Abstract:

Gastrointestinal infections, causing diarrhea, are a global health concern involving parasitic, bacterial, viral, and fungal agents. They can penetrate the mucosal barrier, producing cytokines, chemokines, and antimicrobial compounds. Diagnostic techniques for gastrointestinal infections include blood tests and stool/fecal tests, which detect bacteria, viruses, or parasites in bowel movements. This review delves into various diagnostic methods for gastrointestinal illnesses, as well as gastrointestinal panel PCR detection's ability to rapidly and precisely identify pathogens, which enhances the efficacy of treatment and public health interventions.

Keywords: Gastrointestinal, virus, bacteria, parasite, molecular biology, Culture, serology

Introduction:

Gastrointestinal infections are a prevalent worldwide health issue. They typically cause diarrhea and most frequently impact the stomach or intestines (1). Gastrointestinal infections contain the typical parasitic, bacterial, viral, and fungal agents (2) (Table 1). Most of these microbes are symbionts, also known as commensals, and often do not cause an adverse inflammatory reaction. Nevertheless, infections can penetrate the mucosal barrier and the underlying tissue, causing cytokines, chemokines, and antimicrobial compounds to be produced (3). The microorganisms that cause gastrointestinal infections differ by geographic region, level of economic development, sanitation, and hygiene standards (1). Intestinal infections frequently bring on gut dysbiosis, and numerous studies have linked inflammatory bowel disease, functionally changed commensal bacteria, and intestinal infections (4,5,6). The symptoms of most gastrointestinal illnesses are similar; however, they can differ in intensity. Gastrointestinal infections can cause the following symptoms: stomach cramps, diarrhea, nausea, vomiting, fever, muscle aches, electrolyte imbalance, gas and bloating, and inadvertent weight loss (7).

Bacteria	Virus	Fungal	Parasites
Salmonella spp.	*Cytomegalovirus*	*Candida spp.*	*Cryptosporidium*
Campylobacter spp.	*HIV*	*Histoplasmacapsulatum*	*Giardia lamblia*
Shigella spp.	*Herpes simplex*	*Pneumocystis*	*Microsporidium*
E. coli	*Varicella zoster*	*Cryptococcus neoformans*	*Entamoebahistolytica*
Aeromonas spp.	*HHV-8*	*Aspergillus spp.*	*Leishmania*
Plesiomonasshigelloides	*HHV-6*	*Penicilliummarneffei*	*Strongyloides*
Clostridium difficile	*Adenovirus*	*Zygomycetes*	*Cyclosporacayetanensis*
Listeria monocytogenes	*EBV*		*Isospora belli*
Mycobacterium tuberculosis	*Enterovirus*		
Mycobacterium spp.	*Norovirus/Sapovirus*		
Helicobacter spp.	*Astrovirus*		
Chlamydia trachomatis (LGV)	*Rotavirus*		
	Human papilloma virus		

Table 1: Microbial agents causing more severe or complicated gastrointestinal infection in the immunocompromised host.

Diagnostic Tests for Gastrointestinal Disorders:

Infectious gastroenteritis (IG) is a major global health issue, causing over 1.6 million deaths annually (11). It is particularly prevalent in children under 5 years old, particularly in countries with limited resources (12). IG is the second leading cause of death in this age group. Despite its high socioeconomic impact (13), IG is less common in countries with high resources. IG can be caused by viruses, bacteria, or parasites, with viruses being the most common cause. Traditional diagnosis of IG relies on conventional culture, microscopy, or immunochromatography (ICT) for antigen or toxins detection (14).

Blood tests:

Blood tests are crucial for diagnosing bacterial/parasitic infections, celiac disease, and lactose intolerance. They assess blood count, liver function tests, antibodies, and pancreatic enzyme testing. Liver efficiency tests include complete blood count (CBC), albumin, and liver function tests. Blood tests can also help diagnose gastrointestinal ailments by detecting antibodies or other symptoms of a disease. Serological assays are the most common blood tests. Clostridium difficile (C. diff) tests analyze blood samples to check for antibodies produced by the immune system in response to infection (**Error! Reference source not found.**).

Traditional tests for detecting bacteria:

The stool culture test detects and identifies bacteria that cause illnesses in the lower digestive system (15). The test distinguishes between harmful bacteria and those that are naturally prevalent in the digestive system (normal flora). The test can help establish whether pathogenic germs are causing gastrointestinal symptoms (gastroenteritis) (16). Traditional laboratory-based diagnostic approaches in mycology include microscopy, histology, culture, and serology (17). Conventional culture is a reliable method for diagnosing bacterial entry pathogens, having both advantages and limitations. The cultural technique offers a significant benefit in its distinctiveness. Culture has 100% specificity if the pathogen is not present in healthy people.

Culture's sensitivity varies and might be difficult to discern. The culture technique provides isolates that may be utilized for further testing, including antibiotic susceptibility testing. After using a standard culture procedure, the isolate can be sent to state public health laboratories for further identification, outbreak investigations, and epidemiological research. The disadvantages of the culture approach include low sensitivity and a 3-5-day detection time. It is crucial to highlight that virus, such as norovirus, cause a lot of diarrheas in the population and will not be detected by a bacterial stool culture. Viral investigations on stool specimens are frequently ordered separately.

Traditional tests for detecting viruses:

Electron microscopy (EM) was initially used to identify viral particles in feces samples (18). However, EM observation is seldom utilized as a regular diagnostic technique because of its high cost, competence requirements, and low sensitivity. Seven commercial immunochromatographic techniques were assessed to identify group A rotavirus antigen in human feces samples. Rotavirus, Adenovirus, and Norovirus genogroup I (GI) and genogroup II (GII) antigens were qualitatively detected in human feces in separate bands. These tests demonstrated similar levels of diagnostic accuracy and were appropriate for detecting rotavirus in individuals with acute gastroenteritis, although they missed some asymptomatic rotavirus shedding detected by real-time reverse transcription-PCR (18).

Traditional tests for detecting protozoa:

Entamoebahistolytica is the primary cause of diarrhea in adults, while Cryptosporidium spp. and Giardia duodenalis are common in children, while Blastocystis spp. and Dientemoebafragilis are

common intestinal protozoa (20). Immunodiagnostic tests, including antibody and antigen detection assays, are inexpensive, user-friendly, and fast. Combining these tests with microscopy is more sensitive and specific for diagnosing intestinal protozoan infections (21).

E. histolytica infections can be diagnosed using indirect hemagglutination, indirect immunofluorescence, but ELISA is a popular platform for detecting antigens during intestinal amoebiasis or anti-Entamoeba antibodies during amoebic liver abscess. Monoclonal antibody-based platforms use various *E. histolytica* antigens, such as lectin-rich surface antigen, lipophosphoglycan, and 170-kDa amoebic adherence lectin. Antigen-based tests can differentiate between *E. histolytica* and *E. dispar*, but their sensitivity ranges from 80% to 94% compared to PCR (20). Direct microscopy after concentration with Parasep® tubes using an alcohol-based fixative (Alcorfix®) was used in the laboratory for the microbiological diagnosis of protozoa and other parasites in stool samples, as well as ICT antigen detection of Cryptosporidium spp. and Giardia intestinalis (20). For laboratories with limited capacity for diagnostic complexity, they do not require trained microscopists, or expensive equipment, and can be completed very quickly. Multiplex PCR assays are more sensitive and specific than microscopy in detecting and identifying intestinal protozoa.

Molecular Biology detection:

Molecular methods including reverse transcriptase polymerase chain reaction (RT-PCR) and real-time PCR are extremely sensitive and specific, making them the gold standard for parasite detection, genetic characterization, and epidemiological investigations. RT-qPCR should be considered for detecting low virus loads due to its higher sensitivity (19). Various viruses, bacteria, and parasites can infect the digestive system. Multiplex commercial assays can detect common pathogens (Table 2) in open and closed systems (14). Open assays require separate nucleic acid extraction, while closed assays perform simultaneous extraction, amplification, and product analysis .The gastrointestinal pathogen panel detects the presence of numerous disease-causing (pathogenic) microorganisms in a stool sample. The GI pathogen panel identifies genetic material (RNA or DNA) from some of the most frequent infections. It can detect co-infections (diseases caused by more than one bacterium) and microorganisms that regular testing may miss. The results of a GI pathogen panel may be obtained in a matter of hours, as opposed to days with conventional standard tests. Montessar *et al* compared conventional methods and multiplex-PCR for pathogen detection in 200 patients, finding multiplex-PCR more effective for Shigella, *Enterohemorrhagic Escherichia coli*, and *Aeromonas* isolates, but not *Campylobacter*, which was detected only by multiplex-PCR. These tests can identify infections that may or may not be prevalent in a certain area (26). Local epidemiology and institutional needs should be addressed before acquiring them. Assays with independent bacterial, viral, and parasite panels allow physicians to request particular testing. The significance of ongoing surveillance in the context of multiplex PCR testing for proper treatment and future preventative strategies (22). Using a syndromic testing panel can thus offer healthcare practitioners early and accurate information, allowing for.

Table 2: Gastro-panel PCR test detects several pathogens.

Virus	**Bacteria**	**Parasite**
Sapovirus (I, II, IV, V)	*Clostridium difficile toxin A/B*	*Entamoebahistolytica*
Astrovirus	*Campylobacter (C. jejuni, C. upsaliensis, C. colis, C. lari)*	*Cryptosporidium spp*
Rotavirus A	*Salmonella spp*	*Giardia lamblia*
Norovirus GI	*Escherichia coli VTEC (E. coli STEC (STX1/STX2))*	
Norovirus GII	*Escherichia coli EIEC/Shigella*	
Adenovirus	*ersiniaenterocolitica*	
	Escherichia coli EAEC	
	Escherichia coli STEC O157:H7	
	Plesiomonasshigelloides	
	Vibriocholerae	
	Vibrioparahaemolyticus	
	Vibriovulnificus	

The impact of PCR on improving enteric pathogen detection in Lebanon:

Certain laboratories in Lebanon have a molecular biology section. In the past, not all diagnostic laboratories could do molecular research, which required expensive equipment and extensive technical understanding. Many Lebanese investigations revealed a significant incidence of gastroenteritis. Ghssein *et al.* demonstrated in 2018 that *E. histolytica* infection is the largest cause of pediatric gastroenteritis in hospitalized children discovered using a standard laboratory approach, with 42.4% of the pathogens remaining unidentified, underlining the need for novel laboratory diagnostic methods (23). Viruses, notably rotavirus and adenovirus, are becoming more commonly discovered as diagnostic tools improve. Due to the high frequency of viral diarrhea among the pediatric age group in our region, especially rotavirus and adenovirus, combined with the accompanying non-specific indications and symptoms, we strongly advise medical laboratories to have viral detection equipment (24). Between March and May 2020, 47 laboratories around the country participated in COVID-19 testing (25), which resulted in the opening of a new molecular biology department and the ability to test various epidemiological factors, including gastro infection. Because of the high throughput of stool screening and the large number of potential enteric pathogens, a molecular method based on target multiplexing is required (26). Gastroenterologists must plan a new diagnostic method to provide the patient with appropriate therapy while also avoiding the use of antibiotics that are not specific to the parasite (27, 28, 28).

Conclusion:

Multiplex PCR is a reliable and fast approach for detecting common intestinal pathogens that cause severe gastroenteritis. a quick approach that might be utilized in outbreaks to diagnose the major enteric pathogen that causes deadly gastroenteritis. Using a gastro panel can thus offer healthcare practitioners early and accurate information, allowing for more effective treatment and public health actions. The rising availability of molecular tests may discover diseases that would have been impossible to detect using traditional methods, and this could be an important component of antimicrobial stewardship programs.

Funding:

Sofia Med Company (Rouba Abboud)

References:

1. Burd, E. M., &Hinrichs, B. H. (2015). Gastrointestinal Infections. *Molecular Pathology in Clinical Practice*, 707–734. https://doi.org/10.1007/978-3-319-19674-9_50
2. von Rosenvinge, E. C., Song, Y., White, J. R., Maddox, C., Blanchard, T., & Fricke, W. F. (2013). Immune status, antibiotic medication and pH are associated with changes in the stomach fluid microbiota. *The ISME journal*, *7*(7), 1354–1366. https://doi.org/10.1038/ismej.2013.33
3. Belkaid, Y., & Hand, T. W. (2014). Role of the microbiota in immunity and inflammation. *Cell*, *157*(1), 121–141. https://doi.org/10.1016/j.cell.2014.03.011
4. Yang, W. H., Heithoff, D. M., Aziz, P. V., Sperandio, M., Nizet, V., Mahan, M. J., &Marth, J. D. (2017). Recurrent infection progressively disables host protection against intestinal inflammation. *Science (New York, N.Y.)*, *358*(6370), eaao5610. https://doi.org/10.1126/science.aao5610
5. Axelrad, J. E., Joelson, A., Green, P. H. R., Lawlor, G., Lichtiger, S., Cadwell, K., &Lebwohl, B. (2018). Enteric Infections Are Common in Patients with Flares of Inflammatory Bowel Disease. *The American journal of gastroenterology*, *113*(10), 1530–1539. https://doi.org/10.1038/s41395-018-0211-8
6. Mylonaki, M., Langmead, L., Pantes, A., Johnson, F., &Rampton, D. S. (2004). Enteric infection in relapse of inflammatory bowel disease: importance of microbiological examination of stool. *European journal of gastroenterology&hepatology*, *16*(8), 775–778. https://doi.org/10.1097/01.meg.0000131040.38607.09
7. Gastrointestinal infection: Symptoms, types, and treatment
8. Diagnostic Tools for Detecting GI Infections IFFGD.Sepideh Mehravar, MD, Postdoctoral Researcher, Cedars-Sinai Medical Center. Edited by Ali Rezaie, MD, MSc, FRCPC, Associate Professor, Cedars-Sinai Medical Center.
9. Muzammil, M. A., Fariha, F., Patel, T., Sohail, R., Kumar, M., Khan, E., Khanam, B., Kumar, S., Khatri, M., Varrassi, G., &Vanga, P. (2023). Advancements in Inflammatory Bowel Disease: A Narrative Review of Diagnostics, Management, Epidemiology, Prevalence, Patient Outcomes, Quality of Life, and Clinical Presentation. *Cureus*, *15*(6), e41120. https://doi.org/10.7759/cureus.41120
10. Holtmann, G., Shah, A., & Morrison, M. (2017). Pathophysiology of Functional Gastrointestinal Disorders: A Holistic Overview. *Digestive diseases (Basel, Switzerland)*, *35 Suppl 1*, 5–13. https://doi.org/10.1159/000485409
11. GBD 2016 Diarrhoeal Disease Collaborators. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of diarrhoea in 195 countries: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Infect Dis. 2018; 18:1211–28. https://doi.org/10.1016/S1473-3099(18)30362-1
12. GBD 2017 Diarrhoeal Disease Collaborators. Quantifying risks and interventions that have affected the burden of diarrhoea among children younger than 5 years: an analysis of the Global Burden of Disease Study 2017. Lancet Infect Dis. 2020; 20:37–59. https://doi.org/10.1016/S1473-3099(19)30401-3.
13. Scallan E, Griffin PM, Angulo FJ et al. Foodborne illness acquired in the United States--major pathogens. Emerg Infect Dis. 2011; 17:7–15. https://doi.org/10.3201/eid1701.p11101.
14. Amjad M. An overview of the molecular methods in the diagnosis of gastrointestinal infectious diseases. Int J Microbiol. 2020; 2020:8135724. https://doi.org/10.1155/2020/8135724.
15. Humphries RM, Linscott AJ. Practical Guidance for Clinical Microbiology Laboratories: Diagnosis of Bacterial Gastroenteritis. Clin Microbiol Rev. 2015 Jan;28(1):3-31. doi: 10.1128/CMR.00073-14. PMID: 25567220; PMCID: PMC4284301.
16. Lee, J. Y., Cho, S. Y., Hwang, H. S. H., Ryu, J. Y., Lee, J.,

Song, I. D., Kim, B. J., Kim, J. W., Chang, S. K., & Choi, C. H. (2017). Diagnostic yield of stool culture and predictive factors for positive culture in patients with diarrheal illness. *Medicine*, *96*(30), e7641. https://doi.org/10.1097/MD.0000000000007641

17. Ashbee H.R. Manual of Clinical Microbiology. ASM Press; Washington, DC, USA: 2015. General Approaches for direct detection and identification of fungi; pp. 1965–1983. [Google Scholar]
18. Soltan, M. A., Tsai, Y. L., Lee, P. A., Tsai, C. F., Chang, H. G., Wang, H. T., & Wilkes, R. P. (2016). Comparison of electron microscopy, ELISA, real time RT-PCR and insulated isothermal RT-PCR for the detection of Rotavirus group A (RVA) in feces of different animal species. *Journal of virological methods*, *235*, 99–104. https://doi.org/10.1016/j.jviromet.2016.05.006
19. Kaplon J, Fremy C, Pillet S, Mendes Martins L, Ambert-Balay K, Aho SL, Pothier P. Diagnostic Accuracy of Seven Commercial Assays for Rapid Detection of Group A Rotavirus Antigens. J Clin Microbiol. 2015 Nov;53(11):3670-3. doi: 10.1128/JCM.01984-15. Epub 2015 Sep 16. PMID: 26378280; PMCID: PMC4609683.
20. Fitri, L. E., Candradikusuma, D., Setia, Y. D., Wibawa, P. A., Iskandar, A., Winaris, N., & Pawestri, A. R. (2022). Diagnostic Methods of Common Intestinal Protozoa: Current and Future Immunological and Molecular Methods. *Tropical Medicine and Infectious Disease*, *7*(10), 253. https://doi.org/10.3390/tropicalmed7100253
21. Parija, S.C.; Mandal, J.; Ponnambath, D.K. Laboratory methods of identification of Entamoeba histolytica and its differentiation from look-alike Entamoeba spp. Trop. Parasitol. 2014, 4, 90–95.
22. Danino D, Hazan G, Mahajna R, Khalde F, Farraj L, Shemer-Avni Y, Greenberg D, Hershkovitz E, Givon-Lavi N, Faingelernt Y. 651. Implementing a Multiplex-PCR Test for the Diagnosis of Acute Gastroenteritis in Hospitalized Children, Are All Enteric Viruses the Same? Open Forum Infect Dis. 2023 Nov 27;10(Suppl 2): ofad500.714. doi: 10.1093/ofid/ofad500.714. PMCID: PMC10678403.
23. Ghssein, G., Salami, A., Salloum, L., Chedid, P., Joumaa, W. H., & Fakih, H. (2018). Surveillance Study of Acute Gastroenteritis Etiologies in Hospitalized Children in South Lebanon (SAGE study). Pediatric gastroenterology, hepatology & nutrition, 21(3), 176–183. https://doi.org/10.5223/pghn.2018.21.3.176
24. Zaraket, R., Salami, A., Bahmad, M., El Roz, A., Khalaf, B., Ghssein, G., &Bahmad, H. F. (2020). Prevalence, risk factors, and clinical characteristics of rotavirus and adenovirus among Lebanese hospitalized children with acute gastroenteritis. *Heliyon*, *6*(6), e04248. https://doi.org/10.1016/j.heliyon.2020.e04248
25. Haddad N, Clapham HE, AbouNaja H, et al. Calculating the serial interval of SARS-CoV-2 in Lebanon using 2020 contact-tracing data. *BMC Infect Dis*. 2021;21(1):1053. doi:10.1186/s12879-021-06761-w
26. Montasser K, Osman HA, Abozaid H, Khalil HS, Hatem Amer W, Sabry AMM. Multiplex PCR: Aid to more-timely and directed therapeutic intervention for patients with infectious gastroenteritis. Medicine (Baltimore). 2022 Oct 14;101(41): e31022. doi: 10.1097/MD.0000000000031022. PMID: 36254068; PMCID: PMC9575839.
27. Semret, M., Schiller, I., Jardin, B. A., Frenette, C., Loo, V. G., Papenburg, J., McNeil, S. A., & Dendukuri, N. (2017). Multiplex Respiratory Virus Testing for Antimicrobial Stewardship: A Prospective Assessment of Antimicrobial Use and Clinical Outcomes Among Hospitalized Adults. *The Journal of infectious diseases*, *216*(8), 936–944. https://doi.org/10.1093/infdis/jix288
28. Branche, A. R., Walsh, E. E., Vargas, R., Hulbert, B., Formica, M. A., Baran, A., Peterson, D. R., & Falsey, A. R. (2015). Serum Procalcitonin Measurement and Viral Testing to Guide Antibiotic Use for Respiratory Infections in Hospitalized Adults: A Randomized Controlled Trial. *The Journal of infectious diseases*, *212*(11), 1692–1700. https://doi.org/10.1093/infdis/jiv252
29. Mohtar, J., Mallah, H., Mardirossian, J.M. et al. Enhancing enteric pathogen detection: implementation and impact of multiplex PCR for improved diagnosis and surveillance. BMC Infect Dis 24, 171 (2024). https://doi.org/10.1186/s12879-024-09047-z