LABORATORY DIAGNOSTIC METHODS FOR CLOSTRIDIOIDES DIFFICILE INFECTION

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Introduction. *Clostridioides difficile* is an anaerobic gram-positive, sporeforming, toxin-producing bacillus that is transmitted among humans through the fecal-oral route, as a result of ingestion of spores. Colonization of *C. difficile* is prevented by barrier properties of the fecal microbiota; weakening of this resistance by antibiotics is a major risk factor for disease. Toxin production is the key to pathogenesis, which leads to colonocyte death, loss of intestinal barrier function, and neutrophilic colitis. *C. difficile* infection is one of the most common healthcare-associated infections mainly occurring in developed countries. It is also estimated that 75% of antibiotic-associated colitis cases are caused by *C. difficile*, and of those, 90–100% are pseudomembranous colitis. In the USA, *C. difficile* has become a major healthcare problem with an estimated half a million infections and 14.000 deaths each year; which can also cause major economic problems in the healthcare system. Due to the rapid evolution of antibiotic resistance in *C. difficile* and the consequent effects on the prevention and treatment of *C. difficile* infection, it is very critical to diagnose patients as soon as possible.

The aime of the study was to carry out an analysis of the performance of current laboratory diagnostic methods for *C. difficile* infection.

Material and methods. We performed systematic review of studies in PubMed and Web of Science. The following methods were evaluated glutamate dehydrogenase (GDH) enzyme immunoassays (GDH EIAs), toxin A and B detection by enzyme immunoassays (toxin AB EIAs), and nucleic acid amplification tests (NAATs) for *C. difficile* toxin genes. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each method were determinated.

Results. Various methods are used to diagnose *C. difficile* infection, including detection of glutamate dehydrogenase (GDH) – an antigen secreted by *C. difficile* – through enzyme immunoassays (GDH EIAs), detection of toxins A or B of *C. difficile* strains through enzyme immunoassays (toxin AB EIAs), or nucleic acid amplification tests (NAATs) for *C. difficile* toxin genes. Each assay has advantages and disadvantages and exhibits performance differences. Based on 39 studies, the pooled sensitivities/specificities were 92.7%/94.6%, 57.9%/97.0%, and 90.0%/95.8% for GDH EIAs, toxin AB EIAs, and NAATs, respectively, compared with those of toxigenic culture. The pooled sensitivities of automated EIAs were significantly higher than those of non-automated EIAs for both GDH and toxins A and B. The pooled sensitivity of Xpert *C. difficile* was significantly higher than those of other NAATs. PPVs increased as *C. difficile* infection prevalence increased, and NPVs were excellent when *C. difficile* infection prevalence was low; at *C. difficile* infection prevalence of 5%, PPV=37%-65% and NPV=97%-100%; at *C. difficile* infection prevalence of 50%, PPV=92%-97% and NPV=65%-98%.

Conclusions. Accurate diagnosis of *C. difficile* infection is essential as it guides patient management and infection control practices. The data from this study may be useful for *C. difficile* infection diagnosis in clinical microbiology laboratories and for clinicians diagnosing and treating *C. difficile* infection.