2357. Toxin Detection Using Single Molecule Counting Technology: The Best of Both Worlds?  
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Session: 250. HA1: C. difficile - Diagnostic Testing  
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Background. Accurate diagnosis of C. difficile remains challenging as there is no standalone laboratory test with adequate clinical sensitivity and specificity. Thus, many clinical laboratories currently employ a multiplex assay incorporating a sensitive screening test followed by a specific toxin test. An automated ultrasensitive toxin immunoassay (Singulex Clarity) C. difficile toxins A/B assay has demonstrated excellent performance compared with cell cytotoxicity neutralization assay (CCNA). In this study, the Clarity assay was evaluated relative to glutamate dehydrogenase (GDH), toxin EIA, toxin B gene PCR, multistep algorithms, and C. difficile culture with ribotyping.

Methods. Residual clinical stool samples (n = 293) were collected from patients with suspected C. difficile. The samples were tested on-site with GDH (C. DIFF CHEK™-60), PCR (EntericBio realtime™ C. difficile assay), a membrane-type toxin EIA (Tox A/B Quik Chek™), and culture and ribotyping. In total, 188 samples were tested with GDH and 239 samples were tested by PCR. All PCR-positive samples (n = 148) and prospectively tested GDH samples (n = 97) were tested with the toxin EIA. Culture and ribotyping information were available for 205 samples.

Results. Three of the tested samples gave no result using the Clarity assay and were excluded from the analysis. The Singulex Clarity C. difficile toxins A/B assay had high positive percent agreement (PPA) and low negative percent agreement (NPA) compared with toxin EIA and multistep algorithms ending with toxin EIA. The Clarity assay had high NPA and low PPA compared with PCR, GDH, and the multistep algorithm ending with PCR (figure). Less than 70% of the detected C. difficile PCR positive samples had toxins present. There was no difference in toxin concentration between the ribotypes.

Conclusion. The Clarity assay had strong PPA compared with toxin EIA and strong NPA compared with PCR. The low NPA and PPA compared with toxin EIA and PCR, respectively, may reflect the poor sensitivity of current toxin EIA and low specificity of PCR. The Clarity assay detected 30 different ribotype strains, and less than 70% of samples (by PCR) or strains (by ribotyping) had toxins present. The Clarity assay may be considered for use as a standalone test for CDI diagnosis.

Disclosures. All authors: No reported disclosures.

2359. Prospective Feasibility Study for Novel Ultrasensitive Multiplexed Immunoassay for Clostridiodes difficile Toxins A and B  
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Background. The diagnosis of C. difficile infection is challenging. A wide array of diagnostic tests are used in practice; however, each available test has important limitations. We examined the feasibility and analytical performance of a novel ultrasensitive multiplexed immunoassay designed by Meso Scale Diagnostics (MSD) compared with five current diagnostic assays for detection of C. difficile toxin A and B.

Methods. Stool, serum and urine samples from 44 admitted inpatients were collected within 72 hours of a standard of care nucleic acid amplification test (NAAT) result (23 positive, 21 negative). These specimens underwent five standard diagnostic assays: enzyme immunoassay for toxins A and B (EIA), cytotoxin cell assay, bacterial culture isolation, and two different NAATs to determine presence of viable C. difficile cells, toxins, and toxin-encoding genes (Table 1). The concentration (fg/mL) of toxin A and toxin B in all stool samples was then quantified using MSD’s multiplexed immunoassay (Table 1).

Results. At least one of the five standard diagnostic tests for C. difficile was positive in 16 of the 23 clinically positive patients. The MSD multiplex immunoassay detected toxin A and/or toxin B in 15 of these 16 samples and quantified low levels of toxin A in one clinically positive sample that was negative for all other tests. In contrast, only 2 of the 16 positive samples were positive by EIA, demonstrating the benefits of the ultrasensitive assay over standard immunoassay methods. All clinically negative specimens were negative in all tests. Toxin detection in urine and serum samples was negligible. In stool samples, the MSD test had an estimated sensitivity of 93% (95% CI: 70–99%) and specificity of 93% (95% CI: 78–98%) compared with the clinically used NAAT.

Conclusion. The MSD multiplex toxin assay is a feasible test to move forward for further evaluation. Ultimately, future studies should evaluate the performance of the test compared with standard of care in a prospective randomized trial assessing clinical outcomes.

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