



EVALUATION OF THE NEW VIDAS™ GDH (ELFA) TEST AND VIDAS™ CLOSTRIDIUM DIFFICILE TOXIN A&B TEST COMPARED TO A 3-STEP TOXIN B-PCR BASED-ALGORITHM AT A UNIVERSITY HOSPITAL

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Introduction and Objective

Clostridium difficile, an anaerobic gram positive spore forming rod, is a leading cause of nosocomial infection and one of the most important causative organisms of nosocomial diarrhea.

The diagnosis of *Clostridium difficile* infection (CDI) remains a challenge to both clinicians and microbiologists. Different guidelines suggest various approaches, most of which involve either a 2-step or 3-step algorithm. The tests should be fast and reliable as well as affordable. To respond to this need, GDH-screening tests have been increasingly used in recent years. However, GDH tests show high sensitivity and low specificity, and despite the high negative predictive value, a false positive result often induces unnecessary treatment of CDI. There is therefore a clear need for more accurate and more specific GDH-screening tests.

In addition, rapid diagnosis is important for rapid treatment and immediate initiation of infection control precautions in order to prevent transmission of *Clostridium difficile* spores.

New guidelines have been recently published that include GDH testing. Indeed, the high sensitivity of the GDH assays has led to GDH-testing as the first step in a fixed (3-4 step) algorithm for CDI diagnostics.

The objective of this study was to evaluate our complicated PCR based algorithm used in routine compared to a simple 2-step GDH + Toxin based assay using the new VIDAS GDH combined with VIDAS CDAB when positive.

Material and Methods

Over a period of four weeks (2012-07-24 until 2012-08-17), we analyzed 246 consecutive fresh (<2 h) stool samples of diarrheal patients. Any patients stool specimen from 9 to 93 years of age was included. Stool samples with less than 5 ml were rejected. All samples were analyzed by culture plates and immunoassay tests, defined in our algorithm, including an in-house PCR. (Fig. 1)

The established algorithm consisted of GDH ELISA:

- C. diff. CHEK™- 60 quick ELISA (TECHLAB™; Alere™),
- Rapid membrane enzyme immunoassay for simultaneous detection of *Clostridium difficile* antigen and toxin A&B (TECHLAB™ C.diff QUIK CHEK Complete™; Alere™),
- C.difficile agar (CLO) with cycloserin, cefoxitin and amphotericin B (BioMérieux). Toxins presence on colonies was confirmed using VIDAS CDAB (bioMérieux) and
- Inhouse RT-PCR for detection of the toxin B region (tcdB) only.

In parallel, the new Vidas GDH™ assay and the VIDAS™ C.difficile toxin A&B (CDAB) were performed on VIDAS instrument (BioMérieux – Figure 2)

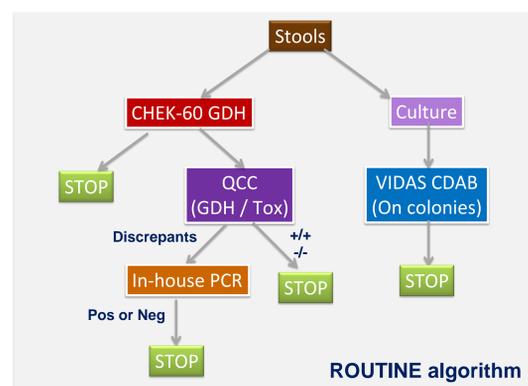


Fig. 1: Established Algorithm August 2012 before introduction of the new test algorithm

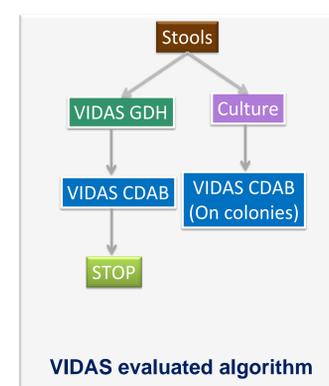


Fig. 2: Evaluated algorithm based on VIDAS GDH + VIDAS CDAB

	Current Laboratory	C.diff Algorithm	bioMérieux algorithm + Vidas CDAB
GDH positive detection	39/246 15,85 % [11,52-21,03]		41/246 16,67 % [12,23-21,92]
GDH + toxins positive detection	11/246 4,47 % [2,25-7,86]		14/246 5,69 % [3,15-9,36]
Positive GDH + toxins detection + complementary tests **	16/246 6,50 % [3,76-10,35]		18/246 7,32 % [4,39-11,32]

**= In House Toxin PCR for current laboratory C.diff algorithm and Vidas CDAB on colonies for bioMérieux algorithm

Table 1: Percentage of positivity for each algorithms for the different steps of diagnosis

GDH	C. diff CHEK - 60 (Alere)	Vidas GDH (bioMérieux)	Agreement (%) IC 95%
Positive Samples (N)	39	41	95,12 % [83,47-99,40]
Negative Samples (N)	235	232	99,03 % [96,55-99,88]

Table 2: Agreement between C diff CHEK-60 (Alere) and VIDAS GDH for GDH detection

GDH + Toxins detection	C.diff Quik Chek Complete (Alere)	Vidas GDH + Vidas CDAB	Agreement (%) IC 95%
Positive Samples (N)	11	14*	78,57 % [49,20-95,34]
Negative Samples (N)	235	232	98,72 % [96,31-99,74]

*= on these 3 samples, 2 are positive with In House Toxin PCR and with Vidas CDAB performed on colonies

Table 3: Agreement between Alere algorithm and VIDAS algorithm

GDH + toxins + complementary tests**	C.diff Quik Chek Complete (Alere) + Toxin PCR	Vidas GDH + Vidas CDAB + Vidas CDAB on colonies	Agreement (%) IC 95%
Positive Samples (N)	16	18	88,89 % [65,29-98,62]
Negative Samples (N)	230	228	99,13 % [96,89-99,89]

Table 4: Agreement between Alere algorithm and VIDAS algorithm with complementary tests

Results

246 stool samples received from patients of the university hospital of Salzburg (Austria) were analyzed. Median age of patients was 51 years, range 9-93. 57,85% of patients were female. Out of 246 samples tested, 192 samples (78%) were negative with both testing procedures.

54 samples (22%) gave a positive result for toxigenic or non-toxigenic *C. difficile* in either one or both of the 2 algorithms. 28 of the 246 samples (11.4%) were only ELISA GDH-Alere positive and 27 (11.0%) only VIDAS GDH positive without toxin confirmation. 11 of the 246 samples (4.5%) were ALERE GDH-toxins positive and 14 (5.7%) were VIDAS GDH and toxins positive. After complementary tests, 16 of the 246 samples (6.5%) were positive with the current Laboratory C. diff Algorithm and 18 (7.3%) were positive with the VIDAS Algorithm (Table 1).

We calculated the positive and negative agreement between both algorithms.

The positive agreement between GDH CHEK-60 (Alere) versus VIDAS GDH was 95.12%. The negative agreement was as high as 99.03%. The confidence intervals suggest that both assays are equivalent (Table 2).

Regarding the toxin component of Alere Quik Chek complete (Alere), it was compared to VIDAS CDAB (bioMérieux). The positive agreement between Quik Chek toxin component versus VIDAS CDAB was 78,57%. Indeed, 3 cases were found positive by VIDAS CDAB and were missed by Alere algorithm (Table 3). The negative agreement was 98,72% without statistical difference.

Regarding both global algorithms, the positive agreement was 88,89%. Indeed, 2 cases were found positive with biomereieux algorithm and were missed with 3-step in-house PCR-based algorithm (Table 4).

Conclusion

In our evaluation, VIDAS GDH (bioMérieux) seems to be equivalent to CHEK-60 ELISA (Alere) with a slight tendency being superior in its negative predictive value.

VIDAS CD A/B showed a significant better positive results compared to the C diff Quik Chek complete (Toxin component).

VIDAS GDH combined with VIDAS CDAB toxin algorithm appears to be superior to the 3-step in-house PCR-based algorithm.

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