MULTI-CENTER PROSPECTIVE VALIDATION STUDY OF A NOVEL Mp1p ANTIGEN ASSAY FOR TALRROMYCOSIS

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BACKGROUND

- Talaromycosis – caused by *Talaromyces marneffei* (Tm) is a leading cause of AIDS deaths in Southeast Asia.
- Blood culture is the mainstay of diagnosis, but culture is positive at very late stage and takes up to 28 days to grow, leading to delayed treatment and higher mortality.
- Objective: We report results of an ongoing multi-center prospective study to determine the diagnostic performance of a novel enzyme immunoassay (EIA) detecting a Tm-specific cell wall mannoprotein Mp1p in patients with advanced HIV disease

METHODS

Figure 1. Study schema



At enrollment

- Hospitalized, HIV positive, age ≥ 18
- CD4 < 100 cells/mm3,
- WHO stage III or IV,
- Not on ART
- ART for ≤ 3 months
- ART for > 12 months

Standard diagnostics
Cultures of blood and other clinical specimens as indicated

Mp1p EIA
(Serum, Urine)

Follow monthly over 6 months

Primary Outcomes
Diagnostic sensitivity, specificity, PPV, NPV, based on ***the gold standard***, defined as incidence of culture-confirmed Tm from any body specimens over 6 months

RESULTS

- 662 patients were enrolled between Feb 2021 and Jan 2023.
- Prevalence of talaromycosis among hospitalized patients with advanced HIV disease is 16.8% (111/662, 95% CI: 14.0% – 19.9%).
- The Mp1p EIA is highly specific at both sites >95%; however, the sensitivity is significantly higher in the southern site compared to the northern site: 92.2% (80.3% - 97.5%) (south) vs. 76.7% (63.75 – 86.2%) (north).
- Overall, the sensitivity of the Mp1p EIA is significantly higher than blood culture in the diagnosis of talaromycosis: 83.8 (93/111, 95% CI: 75.3% - 89.9%) vs 66.7% (74/111, 95% CI: 57.0% – 75.2%), P = 0.002, McNemar's test.

- Talaromycosis accounts for 16.8% (93/662) of hospitalized patients with advanced HIV disease.
- Mp1 EIA is more sensitivity than blood culture (83.8% vs 66.7%), and more sensitive in southern than northern Vietnam (92.2% vs 76.7%).
- Urine is an excellent stand-alone screening test.

RESULTS (Cont.)

Figure 2. OD distribution between Tm and no Tm and diagnostic ROC by study sites

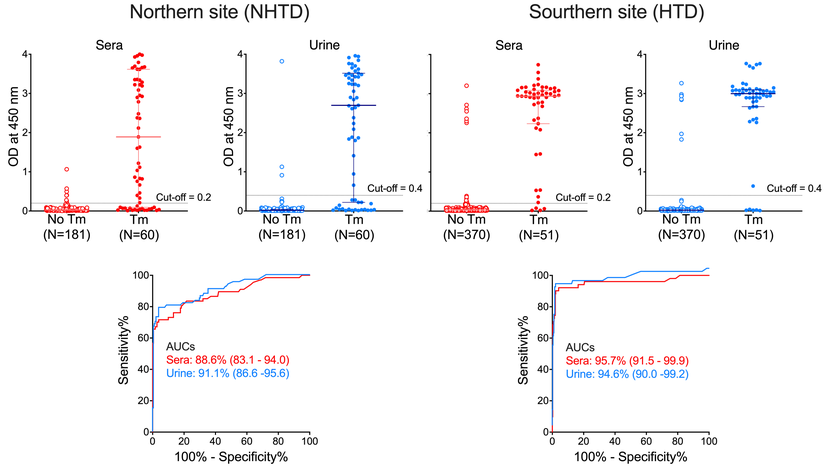


Table 1. Diagnostic performance in serum vs urine samples

	Sera		Urine		Sera + Urine	
	Tm (n=111)	No Tm (n=551)	Tm (n=111)	No Tm (n=551)	Tm (n=111)	No Tm (n=551)
TmAg Pos	91	22	90	11	93	25
TmAg Neg	20	529	21	540	18	526
Sensitivity	91/111 (82.0%, 73.3-88.4)		90/111 (81.1%, 72.3-87.7)		93/111 (83.8%, 75.3-89.9)	
Specificity	529/551 (96.0%, 93.9-97.4)		540/551 (98.0%, 96.3-98.9)		526/551 (95.6%, 93.3-97.0)	
PPV	91/113 (80.5%, 71.8-87.1)		90/101 (89.1%, 81.0-94.2)		93/118 (78.8%, 70.1-85.6)	
NPV	529/549 (96.4%, 94.3-97.7)		540/561 (96.3%, 94.2-97.6)		526/544 (96.7%, 94.7-98.0)	

RESULTS (Cont.)

Table 2. Diagnostic performance in northern vs southern site

	Northern site (NHTD) (n=241)		Southern site (HTD) (n=421)	
	Tm (n=60)	No Tm (n=181)	Tm (n=51)	No Tm (n=370)
TmAg Pos	46	8	47	17
TmAg Neg	14	173	4	353
Sensitivity	46/60 (76.7%, 63.7-86.2) (*)		47/51 (92.2%, 80.3-97.5)	
Specificity	173/181 (95.6%, 91.2-97.9)		353/370 (95.4%, 92.6-97.2)	
PPV	46/54 (85.2%, 72.3-92.4)		47/64 (73.4%, 60.7-83.3)	
NPV	173/187 (92.5%, 87.5-95.7)		353/357 (98.9%, 97.0-99.6)	

(*) NHTD vs HTD TmAg sensitivities, p = 0.05

CONCLUSIONS

- We report a high prevalence of talaromycosis (16.8%) in hospitalized patients with advanced HIV disease.
- The Mp1p EIA is superior to blood culture in sensitivity and is highly specific, making it an excellent rapid rule-in test for talaromycosis, allowing earlier antifungal treatment which can reduce mortality.
- The assay performs well in urine sample alone, unlocking the ability to screen for disease from out-of-hospital settings using a non-invasive sample.

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