Predicting the Risk of Death in HIV-associated *Talaromyces marneffei* Infection

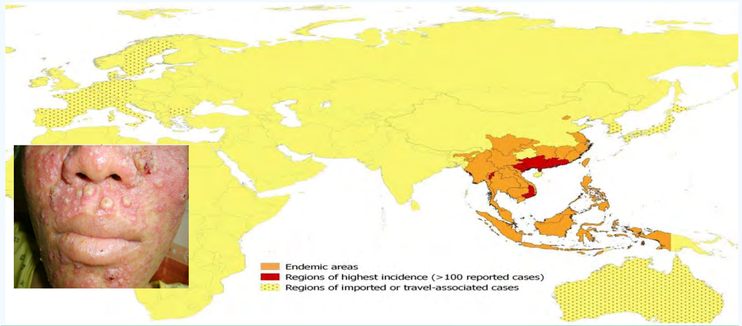
Nguyen Tat Thanh[1], Nguyen Le Nhu Tung[2], Jeremy Day[1], Cecilia Shikuma[3], Nguyen Van Vinh Chau[2], Guy Thwaites[1], Thuy Le [1,3]

[1]Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam; [2]Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam;
[3]Hawaii Center for AIDS, University of Hawaii at Manoa, Honolulu, USA

Background

Disseminated *Talaromyces marneffei* infection (formerly penicilliosis) is the third most common opportunistic infection in Southeast Asia. On treatment mortality is up to 30%. There are no clinical algorithms to predict outcomes.

Geographic Distribution of Talaromycosis



Objective

To develop a model and scoring system to predict death in talaromycosis

Methods

- Study population: Combined data set of culture-confirmed talaromycosis patients from a retrospective cohort 2004-2009 (N=513) and a case-control study 2010-2011 (N=36) from the Hospital for Tropical Diseases in Ho Chi Minh City, Vietnam.
- Primary outcome: in-hospital death or deteriorating clinical status at discharge (who were expected to die at home)
- Covariates: included age, sex, history of injection drug use, comorbidities, clinical and laboratory characteristics on admission
- Statistical analysis: We performed logistic regression analysis with stepwise variable selection. Based on the coefficients of predictors, a prognostic score was developed to estimate the risk of death. Multiple imputation using chained equation (MICE) was applied for missing values (AST missing 19% and creatinine missing 11%). Bootstrap method was used for internal validation of the final model.

Results

- A total of 549 patients with microbiology-confirmed HIV-associated talaromycosis were included in the analysis.
- Poor outcome was observed in 175 (31.9%) patients – 133 (24.2%) died in hospital, 42 (7.7%) were discharged to die at home.

Multivariate complete case analysis (N=389)

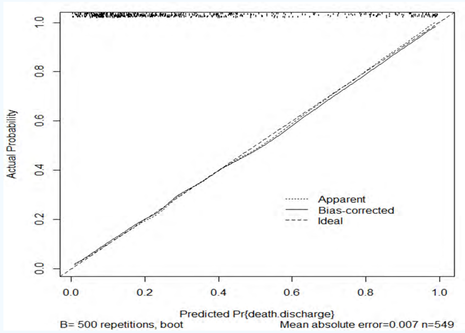
Covariate	Coefficient	OR	95% CI	P value
Days of illness [-7 days]	0.126	1.12	1.03 - 1.21	0.01
Respiratory rate [+10 breaths per minute]	1.094	2.99	2.09 - 4.42	< 0.01
Platelet count [-50 K/mm^3]	0.179	1.16	1.03 - 1.29	0.02
AST > 300 U/L	0.759	2.14	1.15 - 3.95	0.02
Creatinine > 110 µmol/L	1.185	3.27	1.85 - 5.83	< 0.01
Probable TB or on first 2 months of TB therapy	0.993	2.70	0.86 - 8.28	0.08
CNS syndromes	3.025	20.6	7.82 - 65.72	< 0.01

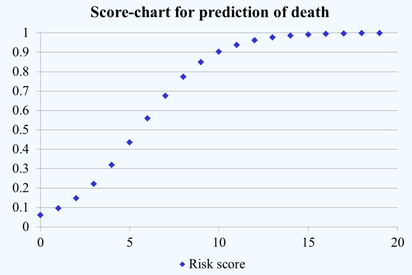
Multivariate analysis with multiple imputation

Covariate	Coefficient	OR	95% CI	P value
Days of illness [-7 days]	0.117	1.11	1.03-1.19	< 0.01
Respiratory rate [+10 per minute]	1.033	2.81	2.02-3.90	< 0.01
Platelet count [-50 K/mm^3]	0.249	1.22	1.11 - 1.32	< 0.01
AST > 300 U/L	0.836	2.31	1.26 - 4.22	< 0.01
Creatinine > 110 µmol/L	0.920	2.51	1.50 - 4.20	< 0.01
Probable TB or on first 2 months of TB therapy	1.159	3.19	1.16 - 8.72	0.02
CNS syndromes	3.351	28.53	10.31 - 78.88	< 0.01

Risk score for prediction of death (complete case analysis)

Covariate	Subcategory	Reference values	Sub-coefficient	Risk score
Days of illness (days)	<7	-	0.474	1
	≥7	Reference	0	0
Respiratory rate (per minute)	≤22	Reference	0	0
	>22 to ≤32	-	0.673	2
	> 32	-	2.360	5
Platelet count (K/mm^3)	<50	-	0.496	1
	≥50	Reference	0	0
AST (U/L)	< 300	Reference	0	0
	≥ 300	-	0.765	2
Creatinine (µmol/L)	<110	Reference	0	0
	≥110	-	1.053	2
Probable TB or on first 2 months of TB therapy	No	Reference	0	0
	Yes	-	1.046	2
CNS syndromes	No	Reference	0	0
	Yes	-	2.950	6
Intercept	-	-	-2.741	-





The internal validation with bootstrap method (500 times) showed acceptable discrimination (AUC=0.68) and calibration slope (0.93). The Brier score (measure of variance) was 0.14 (acceptable range: 0.0-0.25)

Conclusion

We developed a simple scoring system that can predict the risk of death in patients with HIV-associated talaromycosis based on routinely measured characteristics on admission.