



# Predictors of virological failure in a Cambodian setting

Sokkab An, M.D

Sihanouk Hospital Center of HOPE (SHCH),  
Phnom Penh, Cambodia

# Introduction

- Low resource setting
  - Challenge of monitoring therapy
  - Routine VL not affordable
  - Suspected (virological) failure based on WHO 2003 clinical and immunological criteria
  - Unknown sensitivity and specificity of WHO clinical and immunological failure criteria

# Objectives

1. To assess sensitivity and specificity of the WHO 2003 guidelines for treatment failure
2. To assess additional parameters as predictors for virological failure

# Methods

- Cross-sectional study: 399 patients included, NNRTI regimen as first line
- Criteria for inclusion for analysis:
  - Age > 18 years
  - On first line HAART more than 6 months
  - Followed up in SHCH

# Methods

## 1. Validity of WHO criteria (2003)

- Reference (“gold” standard): detectable VL > 50 copies/ml (Roche Amplicor)
- Clinical failure:
  - Onset or recurrence of WHO stage III/IV conditions after the first 6 months of HAART (excluding TB)
- Immunological failure:
  - CD4 decrease to pre-therapy baseline or below
  - Decline > 50% from peak level

# Methods

## 2. Predictors for virological failure

- Outcome:
  - VL > 50 copies/ml
- Possible predictors:
  - $\Delta$ CD4,  $\Delta$ TLC,  $\Delta$ Hgb,  $\Delta$ BMI
  - PPE
  - ART experience, number of switches, adherence, time on ART
  - Gender and age

# Methods

## Statistical analysis

- Continuous variables categorized by ROC analysis:
  - $\Delta$ CD4,  $\Delta$ TLC,  $\Delta$ Hgb,  $\Delta$ BMI
- Multivariate model building using logistic regression

# Baseline results

**Table 1: Baseline characteristics ( N= 399)**

Variable	
Male n (%)	197 ( 49.4)
% WHO stage III	47.6%
% WHO stage IV	36.8%
Median age (IQR)	34 (30 – 39)
Median BMI (IQR)	19 (17 – 21)
Median CD4 (IQR)	52 (13 – 131)
ART regimen	
NVP based	338 (84.7)
EFV based	60 (15)
Other	1 (0.3)

# Results at time of VL

**Table 2: Patient characteristics at time of VL (N=399)**

Variable	
Patient with VL > 50 copies/ml (%)	33 (8.3)
Median time between start ART & VL (IQR)	12.8 (10.7-19.5 months)

# 1. Results

## Validity of WHO failure criteria

**Table 3: Validity of WHO 2003 failure criteria**

	WHO failure Criteria (2003)		
	Clinical	Immunological	Combined Clinical & Immunological
Sensitivity	18%	18%	30%
Specificity	91%	98%	89%
PPV	16%	43%	20%
NPV	93%	93%	93%

## 2. Results

# Predictors for virological failure

Table 4: Univariate analysis

Variable	Virological failure	No virological failure	P-value
Median $\Delta$ CD4	-10 cells/mm <sup>3</sup>	+41 cells/mm <sup>3</sup>	< 0.002
Median $\Delta$ TLC	-356 cells/mm <sup>3</sup>	0 cells/mm <sup>3</sup>	< 0.002
Male	25 (75.8%)	172 (47%)	< 0.02
More than 1 switch	6 (18.2%)	24 (6.6%)	< 0.02

## 2. Results - Predictors

**Table 5: Univariate analysis**

<b>Variable</b>	<b>Virological failure</b>	<b>No virological failure</b>	<b>P-value</b>
Median $\Delta$ Hgb	-0.2 g/dl	+0.2 g/dl	Non-significant
Median $\Delta$ BMI	0	0	Non-significant
Median Time on ART	412 days	380 days	Non-significant
ART experience	4 (12.1%)	21 (5.8%)	Non-significant
PPE	5 (15.2%)	42 (11.5%)	Non-significant

## 2. Results - Predictors

### Final multivariate model logistic regression

**Table 6: Multivariate analysis**

<b>Risk factor</b>	<b>Odds Ratio [95% CI]</b>	<b>P-value</b>
<b>Gender</b> (Men vs women)	<b>3.1 [1.3 – 7.3]</b>	<b>0.008</b>
<b>Change in CD4 †</b> (Decrease or stable versus increase)	<b>2.6 [1.2 – 5.6]</b>	<b>0.016</b>
<b>Change in TLC †</b> (Decrease larger than 300 vs smaller decrease or increase)	<b>2.9 [1.4 – 6.3]</b>	<b>0.006</b>

† over the last 6 months before viral load

# Results

**Table 7: “Refined” WHO criteria**

	WHO - 2003 clinical & immunological Failure criteria	WHO - 2003 clinical & immunological Failure criteria combined with $\Delta$ CD4 & $\Delta$ TLC
Sensitivity (%)	30	79
Specificity (%)	89	53
PPV (%)	20	13
NPV (%)	93	96

# Conclusion

- The sensitivity of the 2003 WHO criteria for treatment failure is low in this Cambodian setting.
- Although we noticed a higher sensitivity of “refined” criteria, PPV is still low because of low prevalence of treatment failure.
- High NPV helps to identify patients that might not need a viral load to make a treatment decision.

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