



# Association of **HIV-1 drug resistance mutations** and clinical outcomes among patients with **first-line antiretroviral therapy failure** in the Philippines

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## BACKGROUND

HIV drug resistance mutations affect antiretroviral therapy (ART), leading to disease progression and the development of opportunistic infections.

## METHOD

This retrospective cohort study involved 142 adult patients with treatment failure to first-line antiretroviral therapy.

Drug resistance mutations were determined at the RITM Aids Research Group Clinic. Sociodemographic, clinical, laboratory, and genotypic data were abstracted. HIV subtypes and drug resistance mutations were identified via Sanger sequencing.

Associations between resistance status, occurrence of any infection, and mortality were then examined using chi-square tests and multivariate logistic regression adjusting for key confounders.

## DISCUSSION

Of 142 patients with first-line ART failure, **CRF01\_A subtype predominated** (73%), consistent with the local epidemiologic shift. 52.8% harbored at least one HIV drug resistance mutation.

**NNRTI resistance was most frequent** (94.7%), followed by NRTI (76.0%) and PI (9.3%) resistance. Dual-class resistance (NRTI + NNRTI) occurred in 66.7%.

Drug Class	Mutation	Frequency (n=75)	Percentage
NRTI	M184V	29	38.7%
	K65R	24	32.0%
	Y115F	12	16.0%
	S68G	9	12.0%
	L74I	7	9.3%
NNRTI	K103N	31	41.3%
	V106M	14	18.7%
	Y181C	14	18.7%
	P225H	9	12.0%
	G190A	8	10.7%

**Table 2. Most prevalent HIV Drug resistance mutations identified in the study cohort**

Clinical Outcome	With Resistance (n=75)	Without Resistance (n=67)	p-value	OR (95% CI)
<b>Any Infection</b>	53 (70.6%)	24 (35.82%)	< 0.001	4.32 (2.13-8.73)
<b>Opportunistic Infections</b>	38 (50.6%)	15 (20%)	< 0.001	3.56 (1.71-7.4)
CMV Retinitis	6 (8.0%)	2 (2.99%)	0.213	2.83 (0.55-14.51)
Pneumocystis Pneumonia	7 (9.33%)	4 (5.97%)	0.458	1.62 (0.45-5.80)
Pulmonary TB	24 (32%)	5 (7.46%)	< 0.001	5.84 (2.08-16.38)
Tuberculous Adenitis	8 (10.67%)	3 (4.48%)	0.181	2.55 (0.65-10.03)
Other Co-Infection	15 (20.0%)	9 (12.0%)	0.21	1.61 (0.65-3.97)
<b>All-Cause Mortality</b>	7 (9.33%)	2 (2.99%)	0.141	3.35 (0.67-16.70)
<b>Absence of Opportunistic Infection and Other Co-Infection</b>	15 (20.0%)	41 (61.19%)	< 0.001	0.16 (0.07-0.34)

**Table 1. Association between HIV Drug Resistance and clinical outcomes**

Opportunistic infections were **more common among those with drug resistance** (50.6% Vs. 22.3%; OR 3.56,  $p < 0.001$ ), with **pulmonary tuberculosis most prevalent** (29.3% Vs. 7.4%; OR 5.84,  $p < 0.001$ ). Mortality among resistant patients was 9.3% versus 2.9% in non-resistant group, aligning with analyses showing that **drug resistance significantly increases HIV/AIDS-associated mortality**.

The **K65R mutation was associated with significantly lower odds of PTB** (OR 0.16;  $p = 0.007$ ) and OIs on multivariate analysis (OR 0.27;  $p = 0.013$ ). Dual mutations involving M184V, K103N, and K65R were most observed.

## CONCLUSION

**Dual-class resistance driven by M184V, K103N, and K65R dominated first-line ART failures and was strongly associated with opportunistic infections – particularly tuberculosis – and mortality.** These findings underscore the need for routine viral-load monitoring, subtype-aware genotypic interpretation, rapid transition to high-barrier regimens, integrated TB screening and prophylaxis, and strengthened adherence support for high-risk patients.

