Clinical Outcomes of Immune Nonresponse Among Virally Suppressed Adults Living with HIV in Thailand

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BACKGROUND

Despite effective antiretroviral therapy (ART) and achieving virological suppression, a minority of adults living with HIV/AIDS (PLWHA) experience poor CD4+ T cell recovery, known as immune non-response (INR). The clinical outcomes for this population, particularly in relation to serious non-AIDS-related events (SNAE), remain poorly understood due to the challenges in controlling confounding factors across multiple cohorts. This study assessed INR clinical outcomes, focusing on SNAE in PLWHA on ART with virological suppression.

METHODS

We conducted a multicenter, retrospective cohort study across three tertiary hospitals in Thailand. PLWHA aged ≥ 20 years, who received ART, had at least two consecutive HIV-1 viral load tests, and were followed for at least 24 months between January 1997 and March 2023 were included. The primary outcome was the incidence of SNAE between the INR group (CD4 < 350 cells/μL after sustained viral suppression (VS) < 50 copies/mL for ≥ 2 years) and a control group with adequate immune recovery.

Immune nonresponse was not associated with an increased incidence of serious non-AIDS-related events among virally suppressed PLWHA

RESULTS

- Between January 1997 and March 2023, 1,596 PLWHA met the eligibility criteria. After excluding cases with a follow-up period of less than two years, 1,457 PLWHA were included in the analysis.
- The incidence of **SNAE was 34 (7.9%) in the INR group compared to 61 (6.0%) in the control group** [crude HR 1.20, 95% CI 0.79-1.82, p=0.406].
- Significant risk factors for SNAE included older age, underlying diseases, male sex, smoking, and a longer time to achieve virological suppression. However, after adjusting for these factors, INR was not significantly associated with SNAE (adjusted HR 1.14, 95% CI 0.74-1.76, p=0.541).
- The Kaplan–Meier curves demonstrated the time to incident SNAE after sustained VS. as cumulative incidence, stratified by immune response status, age at ART initiation, and CD4 level at the time of sustained VS. Age over 50 years at ART initiation revealed a significantly increased incidence of SNAE, while immune response status and CD4 level did not show significant differences.

CONCLUSIONS

INR was not associated with an increased incidence of SNAE. This suggests that while INR is an important immunological marker, it may not independently predict serious non-AIDS-related outcomes in PLWHA with sustained virological suppression.

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Baseline characteristics and outcomes of INR and controls among virally suppressed adults PLWHA

Characteristic and Outcome	INR (n=433)	Control (n=1,024)	*p*-value
Characteristic			
Male sex	345 (79.7)	656 (64.1)	0.00050
Urban residence	344 (79.4)	715 (69.8)	0.00100
Age at HIV diagnosis (yrs.)	40.3 (34.4 - 49.4)	36.9 (29.2 - 44.4)	<0.00001
BMI at diagnosis (kg/m^2)	20.8 (18.8 - 23.2)	21.6 (19.4 - 24.1)	0.00009
CD4 at diagnosis (cells/μL)	67 (23 - 163)	242 (101 - 447)	<0.00001
CD4 at sustained VS (cells/μL)	254 (209 - 299)	531 (443 - 667)	N/A
History of smoking (%)	80 (18.5)	160 (15.6)	0.18791
History of alcohol drinking (%)	110 (25.4)	217 (21.2)	0.09745
Underlying disease (%)	387 (89.4)	873 (85.3)	0.03498
Year of starting ART	2011 (2006-2015)	2012 (2007-2015)	<0.00001
Median time to ART initiation (days)	31 (11 - 79)	35 (9 - 150)	0.12073
Median time from ART initiation to sustained VS (yrs.)	2.91 (2.43 - 3.7)	3.1 (2.54 - 4.53)	0.00051
Outcome			
SNAE (%)	**34 (7.9)**	**61 (6.0)**	**0.406**

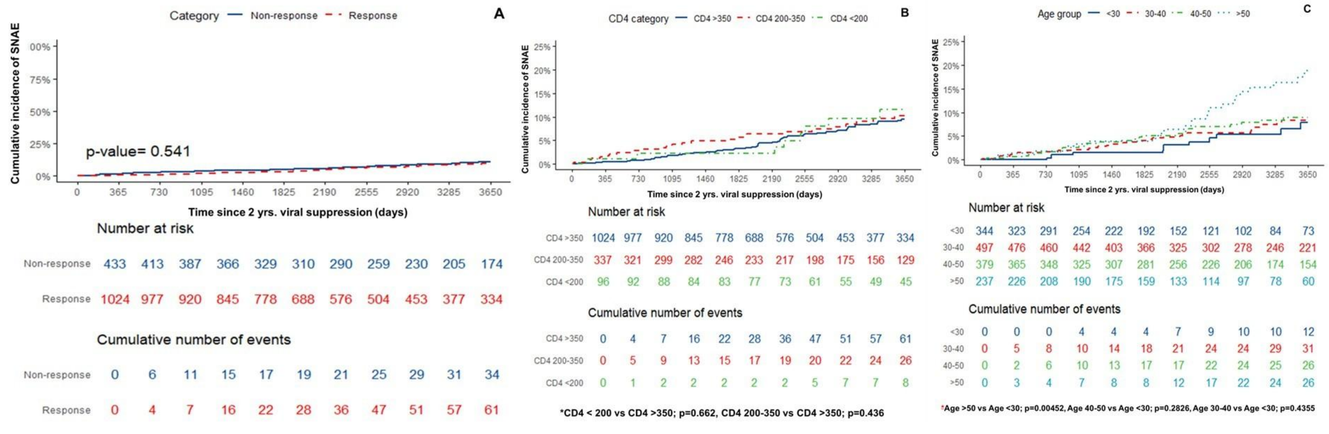


Figure 1 Time-to-incident SNAE

[A] Denotes the difference in time to SNAE by INR status, with red representing CD4 ≥ 350 cells/μL and blue representing CD4 < 350 cells/μL at viral suppression. [B] represents the difference by CD4 at the time of sustained viral suppression, with blue representing > 350 cells/μL, red representing 200-350 cells/μL, and green representing < 200 cells/μL. [C] denotes the difference by age, with dark blue representing < 30, red representing 30-40, green representing 40-50, and light blue representing > 50 years at ART initiation.