

The predictors of anaemia in the 1st year of zidovudine-based antiretroviral treatment in HIV patients, Indonesia



Ratnaningrum K¹, Subronto YW¹, Rintiswati N¹, Mathers B², Petoumenos K², Amin J², Kaldor J²

¹Center for Tropical Medicine, Faculty of Medicine Universitas Gadjah Mada Yogyakarta Indonesia,

²The Kirby Institute University of New South Wales Sydney Australia.

Introduction

Zidovudine (ZDV) is one of the first-line antiretroviral treatment (ART) has side effects anaemia.¹ The growing national epidemic HIV including in Indonesia,¹ the number of HIV patients using ZDV regimen,² and there are limited data about anaemia in people with HIV on ZDV in Indonesia make the reason for researchers to conduct studies to determine factors that predict development of anaemia among patients using ZDV.

Methods

A retrospective cohort study conducted using data from medical records, the national ART register, and laboratory data period of January 2008-June 2012 in Dr. Sardjito Hospital.

Adult patients over 17 years of age starting first-line naive ZDV based ART were included and we excluded the patients with have not information haemoglobin levels at the start of ZDV, haemoglobin level at the start of ZDV ≤ 10 g/dL, unknown haemoglobin levels during the follow-up period, women who are pregnant declared at the start of ZDV, or women who are pregnant during the first year period of ZDV. Patient follow-up was censored at the time first detected as anaemia (≤ 10 g / dL)³ or at the first time when ZDV was replaced by another NRTI within 12 months on ZDV.

Data were analyzed using STATA program version 12 with Kaplan Meier and Cox Proportional Hazard methods. The data collection was approved by the Institutional Review Board of Universitas Gadjah Mada and the Institutional Review Board of Dr. Sardjito Hospital.

Results

In this study we found that there were 151 samples with median age was 29 yo (IQR 26-36) and haemoglobin level was 12.8 g/dL (IQR 11.7-14.1). From table 1. we can see the characteristics ZDV-based ART patients.

Table 1. Baseline characteristics of ZDV-based ART patients

Characteristics	All Patients n, %	No anemia (n=114)	Anemia (n=37)
Age (yo)			
18-29	76 (50.33)	58 (50.88)	18 (48.65)
30-39	46 (30.46)	36 (31.58)	10 (27.03)
= 40	29 (19.21)	20 (17.54)	9 (24.32)
Sex			
Male	101 (66.89)	78 (68.42)	23 (61.6)
Female	50 (33.11)	36 (31.58)	14 (37.84)
Educational level^a			
Low (SD/SMP)	42 (27.81)	31 (27.19)	11 (29.73)
High (SMA-Univ)	105 (69.54)	80 (70.18)	25 (67.57)
Risk group^b			
Heterosexual	80 (52.98)	60 (53.63)	20 (54.05)
IDU	25 (16.56)	19 (16.67)	6 (16.22)
MSM	18 (11.92)	16 (14.04)	2 (5.41)
Clinical stage (WHO)^c			
I/II	87 (57.62)	74 (64.91)	13 (35.14)
III/IV	63 (41.72)	39 (34.21)	24 (64.86)
Cotrimoxazole			
No cotrimoxazole	83 (54.97)	67 (58.77)	16 (43.24)
Cotrimoxazole	68 (45.03)	47 (41.23)	21 (56.76)
TB^d			
No TB	121 (80.13)	95 (83.33)	26 (70.27)
TB	27 (17.88)	16 (14.04)	11 (29.73)
Functional status^e			
Working	113 (74.83)	92 (80.70)	21 (56.76)
Ambulatory	33 (21.85)	18 (15.79)	15 (40.54)
Initial CD4 count (cell/mm³)^f			
1-50	64 (42.38)	43 (37.72)	21 (56.76)
51-199	54 (35.76)	40 (35.09)	14 (37.84)
200-349	26 (17.22)	24 (21.05)	2 (5.41)
= 350	2 (1.32)	2 (1.75)	-
Haemoglobin level (g/dL)			
10.1- 12.7	80 (52.98)	52 (45.61)	28 (75.68)
= 12.8	71 (47.02)	62 (54.39)	9 (24.32)

IDU: Injecting Drug User, MSM: men sex men, WHO: World Health Organization, TB: tuberculosis. a,b,c,d,e,f : missing

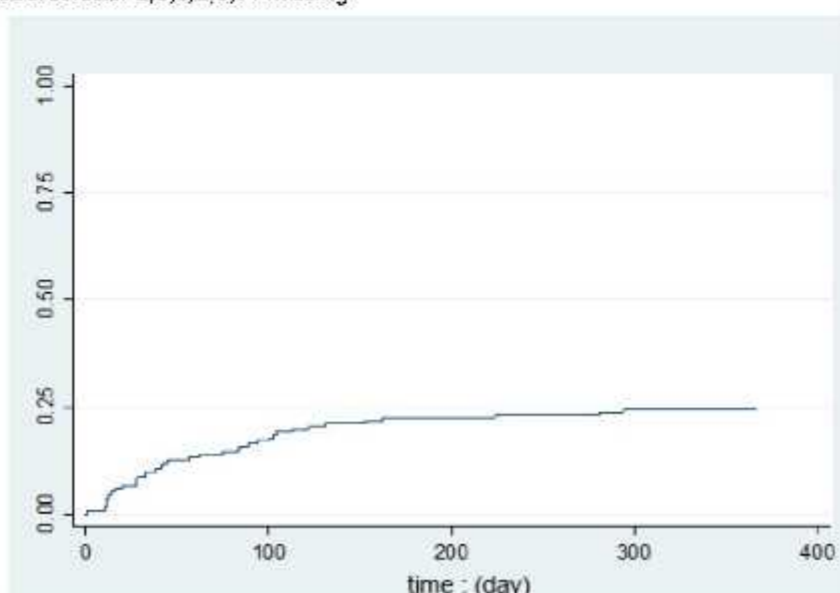


Figure 1. Survival time related anaemia of ZDV-based ART patients

From figure 1 we found that Quartile 25% of observation time of this study can not be estimated due to the low number of patients who related anaemia within 12 months. Anaemia related at first month of ZDV-based ART. Total incidence of 8.3 people per 10,000 person-days of total observation 44.338 people per day.

In this study, clinical stage and haemoglobin level were predictors of ZDV related anaemia within 12 months (Table 2). Advanced clinical stage (stage III or IV) increases the risk of anaemia by 2.42 times compared to stage I or II in the multivariate analysis. Haemoglobin level of 10.1-12.7 g/dL increases the risk of anaemia among patients using ZDV.

Table 2. Factors associated with related of anaemia within 12 months

Characteristics	Crude Hazard Ratio Univariate (95% CI)	P value	Adjusted Hazard Ratio Multivariate (95% CI)	P value
Age (yo)		0.62		
18-29	1.00			
30-39	0.95 (0.44-2.45)			
= 40	1.27 (0.57-2.84)			
Sex		0.90		
Male	1.00			
Female	0.96 (0.49-1.86)			
Educational level		0.47		
Low (SD/SMP)	1.00			
High (SMA-Univ)	0.77 (0.38-1.58)			
Risk group		0.33		
Heterosexual	1.00			
IDU	0.93 (0.37-2.31)			
MSM	0.48 (0.11-2.06)			
Clinical stage (WHO)		0.005		0.01
I/II	1.00		1.00	
III/IV	2.66 (1.35-5.27)		2.42 (1.21-4.83)	
Cotrimoxazole		0.01		0.32
No cotrimoxazole	1.00		1.00	
Cotrimoxazole	2.36 (1.23-4.56)		1.43 (0.70-2.93)	
TB		0.04		0.78
No TB	1.00		1.00	
TB	2.04 (1.01-4.15)		1.11 (0.51-2.39)	
Functional status		0.02		0.08
Working	1.00		1.00	
Ambulatory	2.21 (1.14-4.32)		1.89 (0.91-3.90)	
Initial CD4 count (cell/mm³)		0.002		0.38
1-50	1.00		1.00	
51-199	0.51 (0.25-1.02)		1.4 (0.60-2.99)	
200-349	0.16 (0.04-0.71)		0.41 (0.09-1.84)	
= 350	-		-	
Haemoglobin level (g/dL)		0.002		0.008
10.1- 12.7	1.00		1.00	
= 12.8	0.29 (0.14-0.63)		0.35 (0.16-0.76)	

(-): hazard ratio value is too small

Conclusion

HIV clinical stage and haemoglobin level were the predictors of ZDV related anaemia within 12 months. This result is important for clinician consideration in evaluating Haemoglobin level in the early using zidovudine

Acknowledgements

This study was funded by the Australian Government Department of Foreign Affairs and Trade through the Kirby Institute, Faculty of Medicine, University of New South Wales in collaboration with Faculty of Medicine, Universitas Gadjah Mada.

References

1. Kementerian Kesehatan Republik Indonesia (Kemenkes RI). Pedoman nasional tatalaksana klinis Infeksi HIV dan terapi antiretroviral pada orang dewasa, 2011. Jakarta: Direktorat Jenderal Pengendalian Penyakit dan Penyehatan Lingkungan. 2011.
2. Kementerian Kesehatan Republik Indonesia (Kemenkes RI). Laporan Perkembangan Situasi HIV dan AIDS di Indonesia triwulan 3 September Tahun 2013. Jakarta: Direktorat Jenderal Pengendalian Penyakit dan Penyehatan Lingkungan. 2013.
3. Division of AIDS (DAIDS). Table for Grading the Severity of Adult and Pediatric Adverse Events, clarification August 2009, 1: 1-21.