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Time taken to reach undetectable viral loads in therapy-naïve HIV patients commencing ART

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Abstract

Aims – To assess the proportion of patients achieving undetectable viral loads (<50 copies/mL) within 6 and 12 months of initiating ART in accordance to BHIVA guidelines at a dual-site HIV service in NHS Grampian.
Methods – A retrospective case notes review was conducted of ART-naïve HIV-positive patients attending clinics between January and December 2013. Data collection was performed using a proforma and imported into SPSS 23 for statistical analysis.
Results – A total of 24 case notes were audited (GUM = 15, ID = 9). The median age of patients was 39.5 years (IQR = 24.5 to 54.5), majority male (n = 21/24) and White Scottish (n = 11/24). Median baseline viral load was 77,355 copies/mL while the baseline CD4 count was 382.0. The mean time taken to achieve undetectable viral loads was 4.48 months (95% CI = 3.50 to 5.70). Overall, 70.8% of patients achieved undetectable viral load within 6 months (GUM = 11/15, ID = 6/9). Within 12 months, 95.8% of patients achieved undetectable viral loads (GUM = 15/15, ID = 8/9). A Kaplan-Meier survival analysis showed that patients with a baseline viral load of < 100,000 copies/mL achieved undetectable viral loads sooner compared to those with baseline viral load of > 100,000 copies/mL (3.43 months, 95% CI = 2.337 to 3.663 vs. 6.11 months, 95% CI = 4.28 to 7.94; log-rank p = 0.013).
Conclusions – Achieving undetectable viral loads in HIV patients on ART is a crucial outcome that can significantly improve morbidity and mortality, as well as reduce transmission risk. This audit has identified potential barriers to achieving undetectable viral loads within 6 months, including higher baseline viral load and CD4 count at initiation of ART.

Time taken to reach undetectable viral loads in therapy-naïve HIV patients commencing ART

Introduction

The primary aim of antiretroviral therapy (ART) is the reduction of morbidity and mortality due to chronic HIV infection with minimal drug toxicity.[1] Over the last 15 years, the tolerability of ART has improved significantly and patients on treatment now benefit from improved physical and psychological wellbeing. A further aim of ART is to reduce the risk of HIV transmission and it has been shown to prevent mother-to-child transmission and sexual transmission.[2,3]

In the UK, the overwhelming majority of patients attending HIV services who receive ART experience long-term viral suppression and improved treatment outcomes. Additionally, the life expectancy of people living with HIV (PLWH) on ART has significantly improved, but remains approximately 13 years less than that of the UK population as a whole.[4] A delay in treatment initiation has a significant impact, in that life expectancy is reduced by about 15 years if ART is started later than the current BHIVA guidelines recommend.[4]

Central to ART is the suppression of viral load and this has been used as a means to measure disease burden in PLWH. This variable is used as a proxy for adherence as well as patient prognosis and risk of transmission. Therefore, achieving long-term viral suppression is a key outcome in ART. In this audit, we aim to assess the proportion of

patients achieving undetectable viral load (<50 HIV-1 RNA copies/ml) at 6 months and 12 months, and whether this exceeds 75% in accordance with BHIVA Guidelines.[1]

Standards Set for Audit

1. Proportion of patients achieving undetectable viral loads within 6 months (<50 copies/mL) - 75%.
2. Proportion of patients with a CD4 <350 or <500 with an AIDS-defining illness initiated on ART – 75%
3. Proportion of patients initiating ART containing two nucleoside reverse transcriptase inhibitors (NRTIs) plus one of the following: a ritonavir-boosted protease inhibitor (PI/r), NNRTI, or an integrase inhibitor (INI) – 75%

Methods

A retrospective case note review was performed at the dual-site HIV service in NHS Grampian. All HIV-1-positive patients who were therapy-naïve and commencing ART between January 2013 and December 2013 were included. A data collection proforma was developed and used to extract relevant information which was then imported to SPSS 23 for statistical analysis.

Results

Patient demographics

A total of 24 patients were commenced on ART in the audit time frame. The age, sex, ethnicity, and clinic attended are illustrated in **Table 1**.

Table 1: Socio-demographics of patients.

Aspect	n	%
Age		
26-35	10	41.6
36-45	7	29.2
≥46	7	29.2
Sex		
Male	21	87.5
Female	3	12.5
Ethnicity		
White Scottish	11	45.8
White British	4	20.8
White – Other	2	16.7
Asian	2	8.3
Black African	5	8.3
HIV clinic attended		
GUM	15	62.5
Infection Unit (ID)	9	37.5

ART regimen

The median (minimum, maximum) number of months between diagnosis and commencement of ART was 3.0 (1.0, 109.0). **Figure 1** shows the ART regimens patients were started on. Two patients who commenced on darunavir/ritonavir and emtricitabine/tenofovir were subsequently switched to Eviplera to reduce tablet burden. One patient on Eviplera was switched to Truvada with raltegravir four months after initiation of ART.

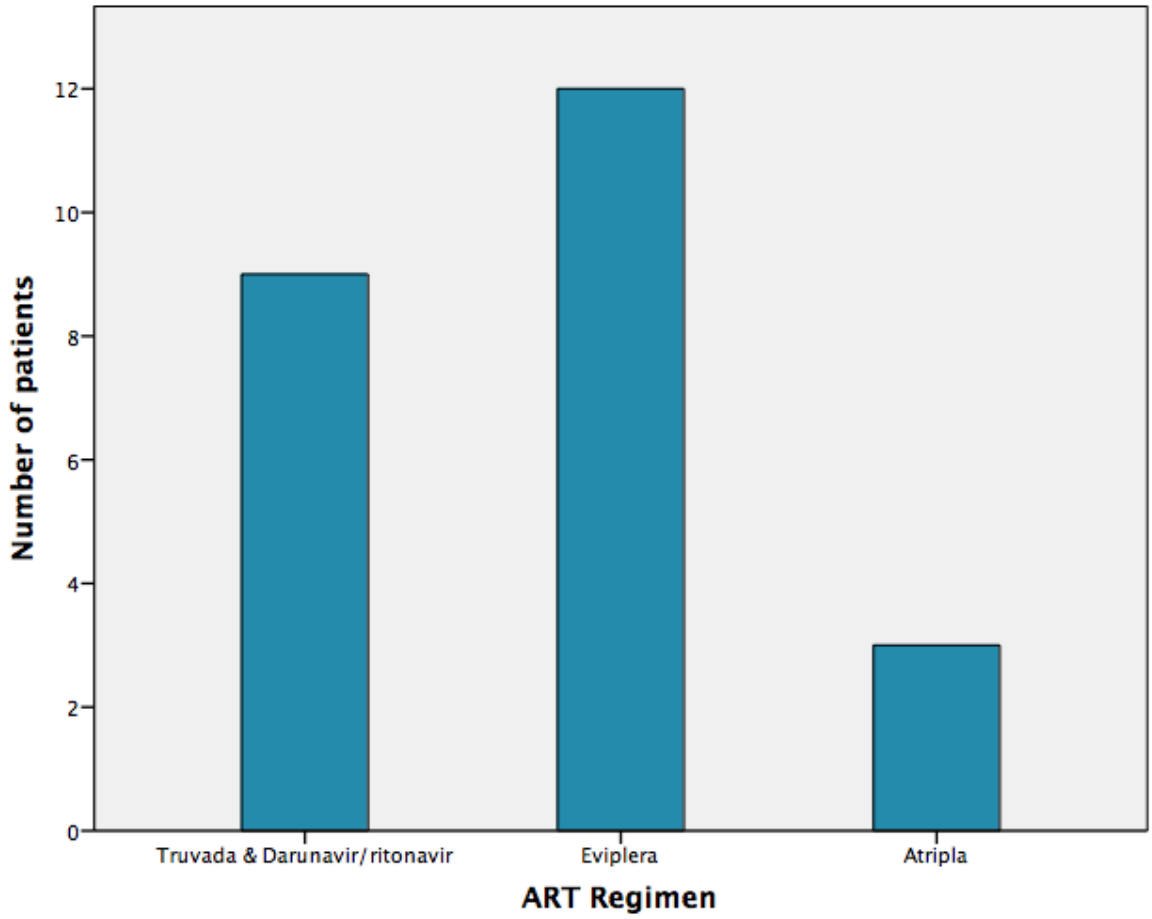

Figure 1 - ART regimen at initiation

HIV viral load and CD4 count

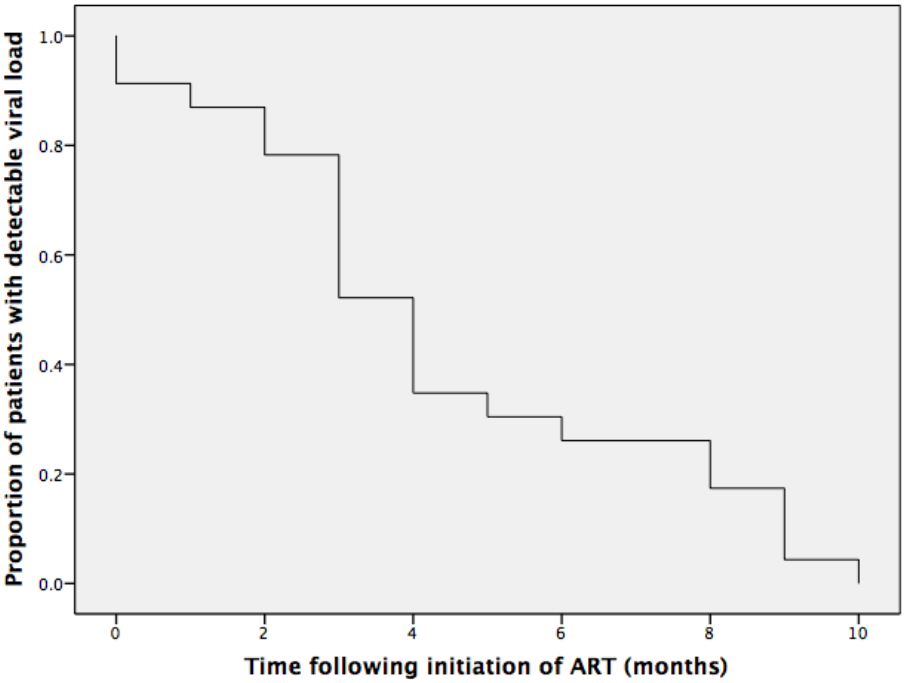

Figure 2 - Survival plot showing proportions of patients with detectable viral load over time

Figure 2 shows the overall Kaplan-Meier survival function for proportions of patients with detectable viral loads over time. The mean time to achieve undetectable viral load is 4.48 months (95% CI = 3.25 to 5.70). Patients with a baseline viral load of below 100,000 copies/mL achieved undetectable viral loads earlier compared to patients with a baseline viral load of more than 100,000 copies/mL (3.43 months, 95% CI = 2.337 to 3.663 vs. 6.11 months, 95% CI = 4.28 to 7.94). Conversely, those initiating ART at CD4 below 350 achieved undetectable viral load later than those initiating at CD4 above 350 (5.37 months, 95% CI = 3.57 to 7.16 vs. 4.14 months, 95% CI = 2.48 to 5.81) (**Figure 3**).

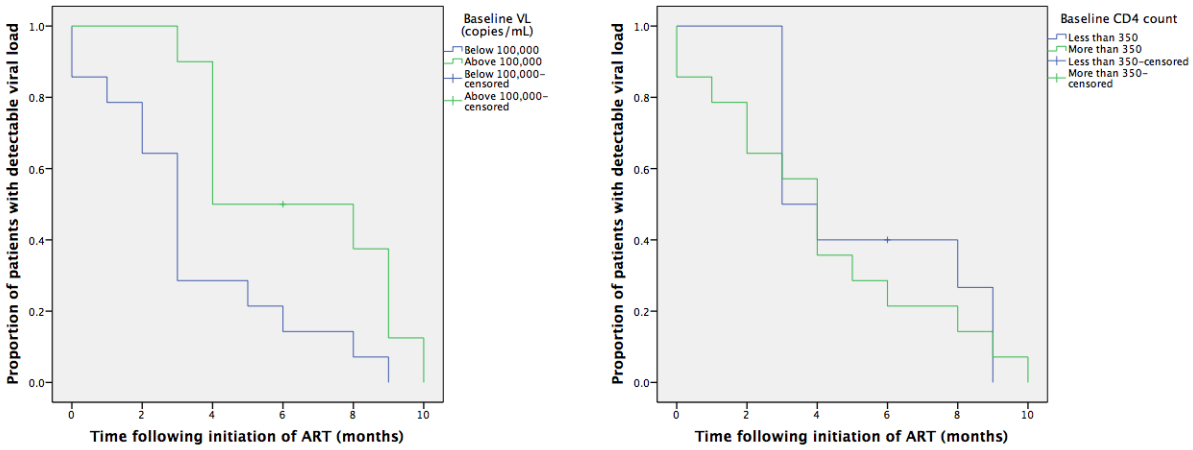

Figure 3 - Survival plot showing proportions of detectable patients over time. (A) Baseline viral load (Log-rank p =0.013); (B) Baseline CD4 count (Log-rank p = 0.50)

Table 2 : Factors influencing proportion of patients achieving undetectable viral loads within 6 months.

Aspect	Undetectable within 6 months, n		χ^2	p-value
	Yes	No		
Age				
26-35	7	3	0.006	0.99
36-45	5	2		
46+	5	2		
Sex				
Male	14	7	1.41	0.53
Female	3	0		
Ethnicity				
White Scottish	8	3	1.58	0.81
White British	3	1		
White - Other	1	1		
Asian	2	0		
Black African	3	2		
HIV clinic attended				
GUM	11	4	0.12	0.73
Infection Unit	6	3		
Time taken between diagnosis and commencement of ART				
Less than 3 months	10	3		
3-6 months	1	2	9.60	0.05
6-12 months	0	2		
1-2 years	1	0		
More than 2 years	5	0		
ART regimen				
Truvada & darunavir/ritonavir	5	4	5.58	0.06
Atripla	1	2		
Eviplera	11	1		

In a Chi-Square analysis of variables measured in this audit, a borderline statistically significant difference was found between groups with variable time taken between diagnosis and commencement of ART (χ^2=9.60, p=0.05). There were no statistically significant differences in time taken to achieve undetectable viral loads in other factors such as age, sex, ethnicity, HIV clinic attended and ART regimen (**Table 2).**

Discussion

The results of this audit found that only 70.8% of patients commenced on ART achieved an undetectable viral load by 6 months, thus failing to achieve the targets recommended by BHIVA. However, it is known that variability between individuals can influence response to treatment, and the fact that 95.8% of patients attending HIV services in NHS Grampian eventually achieve undetectable viral loads within 12 months is reassuring.

One of the limitations of this study is the small sample size that does not allow for conclusions to be made regarding factors that are likely to affect time to undetectable viral loads. Another limitation of the study is a failure to take into account Did Not Attend (DNA) rates as a contributing factor. In our study, it was clear that there were several patients who regularly failed to attend follow-up clinics, as there was missing data for viral load and CD4 measurements for some of the intervals measured. This was, however, not formally quantified. This should be an aspect of future audits or studies within the same area. Another limitation of the study is the poor quantification of adherence rates. ART adherence is a crucial factor in affecting the time taken to reach undetectable viral loads. It is also, unfortunately, a notoriously difficult parameter to measure in clinical practice as it relies on the information that patients volunteer, which may be grossly under- or over-estimated.

Conclusions

Achieving undetectable viral loads in HIV patients on ART is a crucial outcome that can significantly improve morbidity and mortality, as well as reduce transmission risk. This audit has identified potential barriers to achieving undetectable viral loads within 6 months including higher baseline viral load and CD4 count. Furthermore, patients' health-seeking behaviour, i.e. failure to attend follow-up appointments, and poor adherence to medication, may further precipitate treatment failure. These areas need to be addressed to ensure the target of 75% of patients with an undetectable viral load within 6 months of initiating ART can be achieved.

Recommendations

- Continue to encourage patients to attend follow-up as part of routine HIV care and explore different models of care in rural areas i.e. primary care taking viral load samples.
- Adopt an early warning system for patients who are on ART but fail to attend appointments and/or fail to achieve undetectable viral loads by 6 months.
- Consider closer monitoring of patients who start treatment with viral load >100,000 copies.

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