

The impact of HIV-1 infection, combination antiretroviral therapy and ageing on renal function

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Background

The total number of people accessing HIV care in the UK in 2010 was 70,000 (HPA, 2011), and the number of adults living with HIV in the UK (diagnosed and undiagnosed) is estimated to exceed 100,000 by the end of 2012 (HPA, 2011).

The HIV infection rate of people aged 50 and over in England, Wales and Northern Ireland has more than doubled between 2000 and 2007 with a median age at the time of diagnosis of 55 years.

- 299 new cases in 2000.
- 710 new cases in 2007 (Source HPA).

With the increased new cases and success of HIV treatment the ≥ 50 year olds are the fastest growing group of people living with HIV in the UK, and almost three-quarters of new diagnoses within this age group involved individuals aged between 50 and 59.

This may be explained by the success of combination antiretroviral therapy (ART) resulting in longer survival in addition to an increased number of HIV diagnoses in those aged ≥ 50 years.

• Patients with HIV who have been treated long term with combination ART, who subsequently age are at an increased risk of non-AIDS morbidities associated with ageing:

- Cardiovascular disease (e.g. MI).
- Cancer.
- Haematologic disease (e.g. anaemia).
- Neurocognitive decline/impairment (e.g. dementia).
- Bone disease (e.g. osteoporosis).
- Pulmonary disease (e.g. hypertension).
- Liver disease (e.g. fibrosis).
- Kidney disease (e.g. insufficiency).

As age increases renal function declines even in HIV-1 uninfected people. Kidney disease is prevalent in 30% of the population and can cause heart disease, bone disease, lead to early end-stage renal disease or kidney failure, requiring renal transplantation.

In HIV-1 infected patients, renal function deterioration is commonly observed and many published studies have reported deterioration with exposure to:

- Some nucleoside reverse transcriptase inhibitors.
- Some nucleotide reverse transcriptase inhibitors.
- Some protease inhibitors.
- Indinavir.
- Atazanavir.
- Kaletra.

Markers of kidney disease are:

- Creatinine levels in the urine.
- Cystatin C levels in the urine.
- Estimated glomerular filtration rate (eGFR) which is age standardised.

Aims:

This study analysed the relationship between renal function, HIV-1 infection, ARV exposure and increasing age.

The main aims of this study are:

- **firstly** to describe the changing distribution of age over time in our cohort of patients who have been attending for HIV care since the start of the HAART era.
- **secondly** to describe the co-effects of HIV-1, age and exposure to antiretroviral (ARV) drug classes – in particular, NRTI's, PI's and NNRTI's on renal function.

Methods

Study cohort 1st Jan 1988 – May 2011. The age of patients were grouped into categories according to immunological considerations.

• The Chelsea and Westminster HIV cohort was used to investigate the association between HIV-1 infection, exposure to ARV drugs (NRTI, PI and NNRTI) and renal function (measured by eGFR).

• Patient ages are described by:

- Immunological considerations.
 - >40 year.
 - (where decline in thymic function commences on average).
 - >50 years.
 - (coincides with start of immune senescence).
- Decades.

Methods (continued)...

• In the UK the:

- normal age standardised eGFR is >90 ml/min.
- mildly reduced kidney function eGFR between 60 and 90 ml/min is considered stage 2 chronic kidney disease (CKD).

Statistical method:

A random intercept model was generated using MIXED procedure in SAS, fitting all eGFR results as a dependent variable by changing age group strata grouped into decades, and stratified by exposure to ARV drug classes.

The eGFR results were allowed to change in a patient over time and these have been described by age at the time when eGFR result was obtained.

Results

Study cohort

1st Jan 1988 – May 2011

- N = 15,048
- Men – 89%
- Caucasian - 70.7%
- African - 8.8%
- MSM - 81.2%
- IDU - 3.1%

Figure 1: Age distribution shift since the HAART era according to cohort age strata

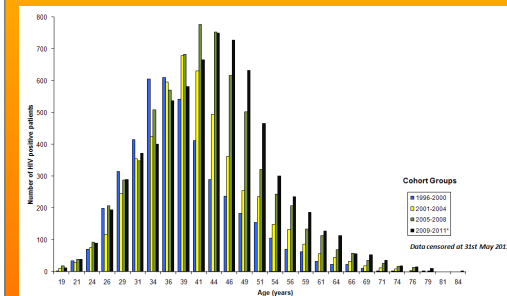
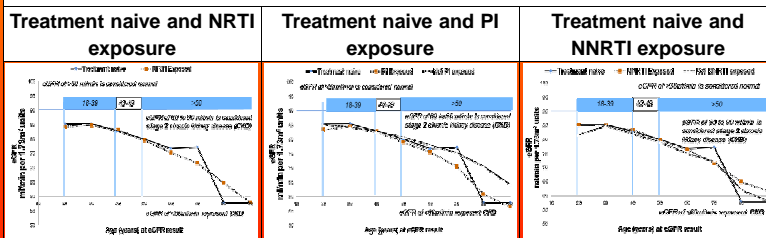


Figure 2:



Conclusion

- Median age increased by 8 years during 15 years of follow-up since the HAART era.
- The mean eGFR reduction by age seen in ART naïve and experienced patients demonstrates renal function deterioration in addition to age related changes.
- Exposure to some ARV drug-classes further adds to the decline in renal function resulting from natural ageing process and HIV-1 infection.
- Success of ART has led to reduced mortality. However, ageing, non-AIDS co-morbidities and, ARV exposure interact with HIV-1 infection effects.
- Further demonstrates co-effects of duration of HIV-1 infection and duration ARV exposure (BHIVA 2012, Oral Abstract # O14, Westrop, SJ et al.).
- As the HIV-1 infected population ages, these conditions will assume even more significance and may warrant novel therapeutic approaches, requiring improved linkage and integration of HIV services with renal services as well as services for other co-morbidities.

Acknowledgements

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