

## ABSTRACT

**Objective:** To describe the incidence of acute renal failure (ARF) and clinical features of patients who developed ARF in a large multi-ethnic cohort of HIV infected patients.

**Methods:** All HIV infected patients who developed ARF at King's College Hospital, London, UK, between 1/1998 and 12/2005 were identified. Serum creatinine and estimated glomerular filtration rate (eGFR) were used to define ARF. ARF episodes were classified as early-onset if they occurred < 3 months of initiating HIV care, and late-onset if they occurred > 3 months after initiating care.

**Results:** During the study period, 130 of 2274 patients (5.7%) developed 144 episodes of ARF. The incidence rates of early-onset and late-onset ARF were 19.3 (15.4-24.1) and 1.1 (0.83-1.49) episodes per 100 person years respectively (rate ratio 17.4, p<0.001). In multivariate analysis, nadir CD4 T-cell count < 100 x 10<sup>9</sup> cells/L (OR 6.7, 2.5-18.3) and AIDS (OR 6.7, 3.4-13.3) were associated with early-onset ARF, while IV drug use (OR 4.8, 1.3-17.7), hepatitis C co-infection (OR 3.4, 1.3-8.6) and nadir CD4 T-cell count < 100 x 10<sup>9</sup> cells/L (OR 5.8, 2.5-13.4) were associated with late-onset ARF.

**Conclusions:** ARF was common and associated with advanced immunodeficiency. The incidence of ARF declined more than 15-fold in patients who had received HIV care for > 3months.

## INTRODUCTION

- Acute renal failure (ARF) is defined as a rapid and usually reversible decline in renal function
- ARF is common in ambulatory HIV infected patients (incidence 5.9 episodes per 100 person years), and more common in hospitalised HIV infected patients in 2003 compared to 1995<sup>(1,2)</sup>
- ARF in the HAART era was associated with advanced HIV infection (CD4 T-cell counts <200 cells/L, HIV RNA levels >10,000 copies/mL, and AIDS), any HAART use and hepatitis C (HCV) co-infection<sup>(1,2)</sup>
- It would appear that the availability of HAART has had little impact on ARF incidence

## METHODS

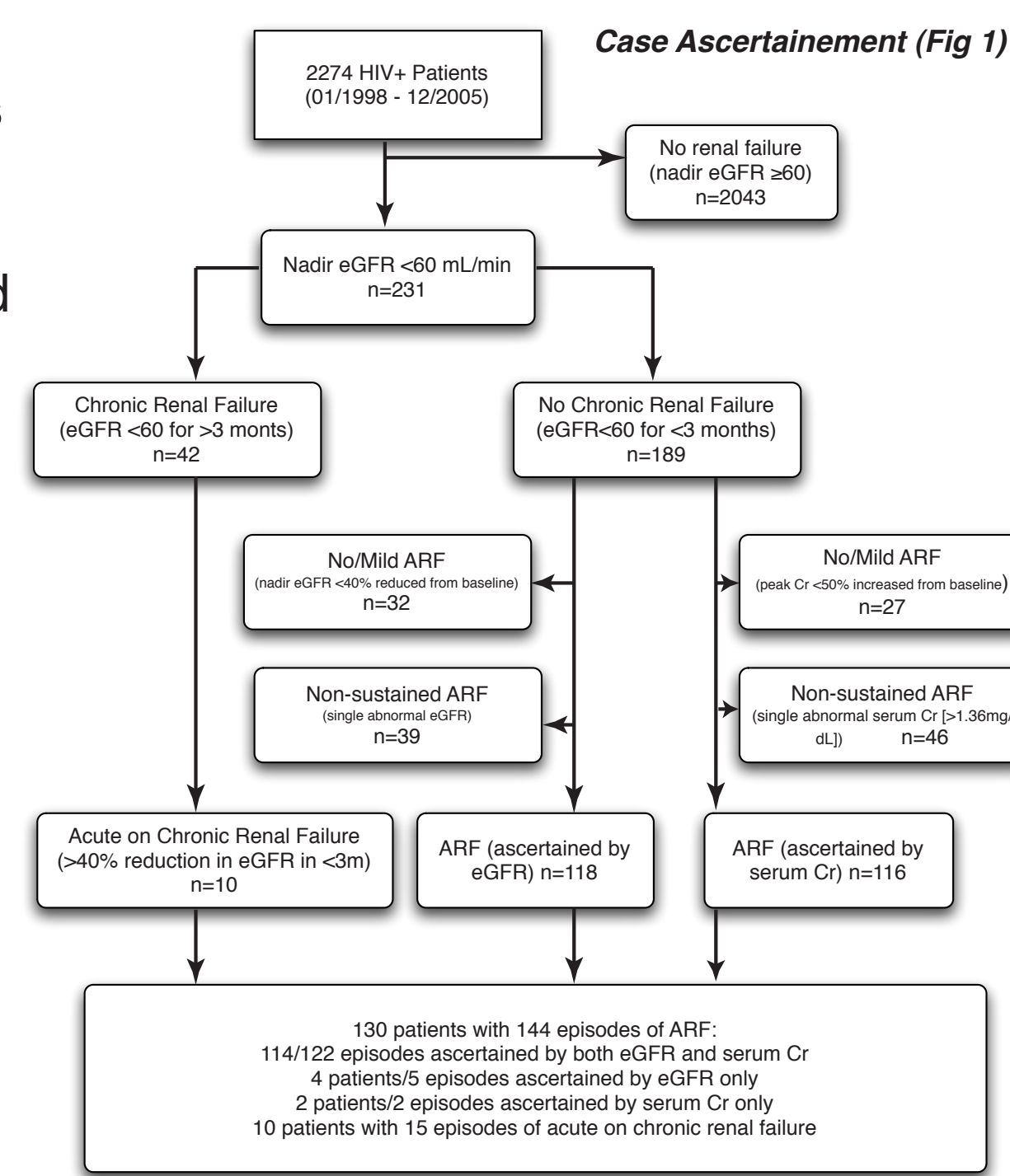
- Review of HIV positive patients aged ≥ 18 years who developed ARF at Kings College Hospital, London, UK
- Study period: January 1998 - December 2005
- Analysis of > 40,000 routinely collected serum creatinine values, converted to eGFR using the MDRD equation
- Acute renal failure was defined as (Fig 1):
  - confirmed eGFR < 60 mL/min
  - nadir eGFR > 40% reduced from baseline
  - ARF duration < 3 months
- or
  - confirmed raised serum creatinine (> 120 μmol/L / 1.36 mg/dL)
  - peak serum creatinine > 50% increased over baseline
  - ARF duration < 3 months

- ARF incidence rate was calculated from date of initiation of HIV care
- ARF episodes were categorised into 'early onset' or 'late onset' in relation to initiation of HIV care (< 3 months or > 3 months from the first visit)
- Logistic regression and Cox proportional hazard models applied to define factors associated with early onset and late onset ARF

## RESULTS

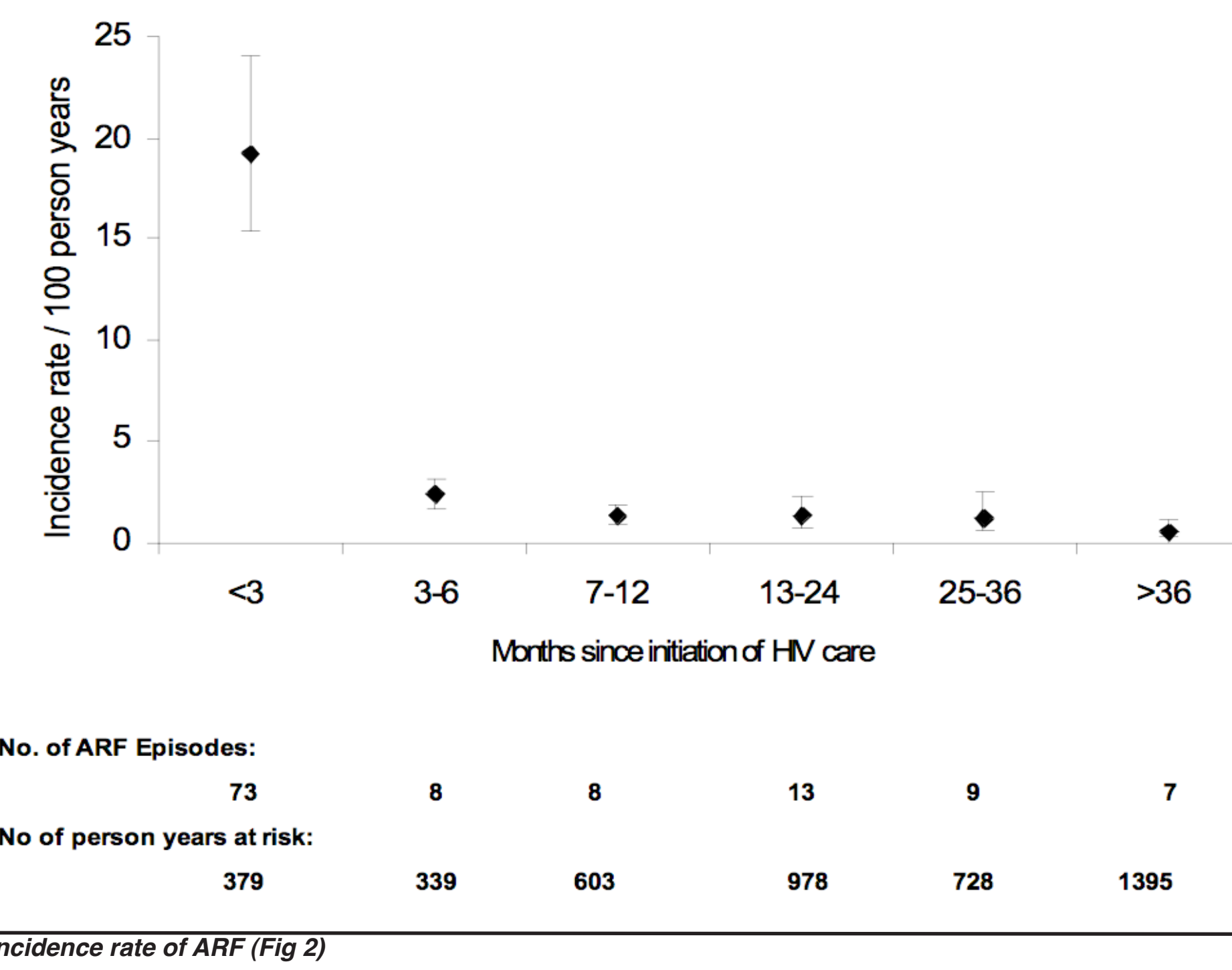
### Patient Characteristics (Table 1)

- 2274 patients, followed for 7394 person years
- Mean age at inception 34.6 years
- 38% female, 58% black, 6% IVDU



### Incidence of ARF (Figure 2)

- 130 patients (5.7%) experienced 144 episodes ARF
- ARF incidence rate 2.7/100 person years
- ~50% of all ARF episodes occurred < 3 months of initiation of care



### Patients with early onset ARF

- ARF was associated with opportunistic infections (55%), other severe infections (36%), malignancy (19%), liver disease (8%), reduced renal blood flow (67%) and/or nephrotoxic medications (73%)
- ARF occurred prior to or during hospitalisation (97%), prior to initiation of HAART (78%), and at low current CD4 count (median 50)
- Median duration of ARF was 8 (IQR 3-31) days; 29% required dialysis, 31% died

### Patients with late onset ARF

- ARF was associated with opportunistic infections (14%), other severe infections (48%), malignancy (14%), liver disease (15%), reduced renal blood flow (73%) and/or nephrotoxic medications (73%)
- ARF occurred prior to or during hospitalisation (93%), while receiving HAART (73%; 45% with HIV RNA < 400 c/mL), and at relatively low current CD4 count (median 162)
- Median duration of ARF was 6 (IQR 2-20) days; 17% required dialysis, 37% died

Of the 20 patients with HCV co-infection

- 1/3 had overt liver disease, 1/3 had infectious complications of IVDU, and 1/3 developed ARF unrelated to HCV/IVDU

### Factors associated with ARF (Table 2)

- In multivariate analysis, nadir CD4 count and AIDS were associated with early-onset ARF, and IV drug use, hepatitis C antibody status, nadir CD4 count and AIDS with late-onset ARF.

	No Renal Failure (n=2043)	ARF (n=130)	p-value	ARF <3 months (n=73)	ARF >3 months (n=57)	P-value
Mean age	34.5	35.9	0.07	34.8	37.1	0.23
Female gender (n, %)	777 (38)	47 (36)	0.67	30 (41)	17 (30)	0.18
Ethnicity* (n, %)			0.11			<0.0001
Black	1161 (58)	84 (64)		60 (82)	24 (42)	
Non-Black	857 (42)	46 (36)		13 (18)	33 (58)	
Risk for HIV* (n, %)			<0.0001			<0.0001
Heterosexual	1171 (61)	81 (65)		60 (87)	21 (38)	
Homo/bisexual	656 (34)	28 (22)		6 (9)	22 (39)	
IVDU	105 (5)	16 (13)		3 (4)	13 (23)	
Nadir CD4 T-cell count (median, IQR)	219 (102-344)	62 (21-158)	<0.0001	38 (13-112)	71 (32-225)	0.009
AIDS (CDC stage C)	354/1752 (20)	78/130 (60)	<0.0001	55 (75)	23 (40)	<0.0001
HBSAg positive (n, %)	82/977 (8)	16/118 (14)	0.06	7 (11)	9 (16)	0.41
HCV Ab positive (n, %)	91/1053 (9)	20/100 (20)	<0.0001	3 (6)	17 (36)	<0.0001
Hypertension (n, %)	64/439 (15)	14/130 (11)	0.49	7 (12)	7 (13)	0.78
Diabetes mellitus (n, %)	10/386 (3)	6/130 (5)	0.17	3 (5)	3 (6)	0.83

Patient characteristics (Table 1)

	Early Onset ARF *			Late Onset ARF **		
	OR	95% CI	P-value	OR	95% CI	P-value
HIV risk						
-Heterosexual	1			1		
-IVDU	0.53	(0.06-4.90)	0.60	4.77	(1.29-17.7)	0.02
-MSM/Bisexual	0.27	(0.09-0.84)	0.02	1.79	(0.67-4.79)	0.24
Ethnicity						
-Non-Black	1			1		
-Black	1.56	(0.54-4.49)	0.41	1.08	(0.41-2.86)	0.87
HCV Ab positive				3.36	(1.31-8.63)	0.01
Nadir CD4						
>200	1			1		
100-199	3.02	(0.99-9.13)	0.05	1.65	(0.60-4.53)	0.34
<100	6.75	(2.5-18.3)	<0.001	5.82	(2.53-13.4)	<0.001
AIDS (CDC-C)						
-CDC stage A/B	1			1		
-CDC stage C	6.72	(3.39-13.3)	<0.0001	2.25	(1.12-4.52)	0.02

\* adjusted for HIV risk group, ethnicity, CD4 T-cell count and CDC-status

\*\* adjusted for HIV risk group, ethnicity, hepatitis C antibody status, CD4 T-cell count and CDC-status

Multivariate Analysis (Table 2)

## DISCUSSION

- The overall incidence of ARF in our cohort was 2.7 episodes / 100 person years, which is lower than reported previously
- The ARF incidence rate was particularly high during the first 3 months following HIV diagnosis / initiation of HIV care
- Beyond the initial 3 months of HIV care, the incidence of ARF was approximately 1 episode per 100 person years
- Our results suggest that HIV care, including targeted HAART and OI prophylaxis, is associated with a marked reduction in the risk of developing ARF
- As nearly all patients with ARF were hospitalised, nephrotoxic antimicrobials should be used judiciously and dehydration and NSAIDs avoided to reduce the risk of ARF in this setting

References:  
1. Franceschini N, et al. Kidney Int 2005;67:1526-31.  
2. Wyatt CM, et al. AIDS 2006;20:561-5.

Funding: Funding for this study was received from GlaxoSmithKline. The funder was not involved in study design, data analysis or interpretation of the results.  
Acknowledgements: Dr Samuel Moses for identifying all patients with positive HIV test results obtained while being admitted to King's College Hospital between 1998 and 2005.