

Death as a serious adverse event

in paediatric antiretroviral therapy patients at Kalafong hospital

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AIM

The aim was to review the serious adverse event, defined as death, in children treated at the paediatric antiretroviral therapy (ART) clinic at Kalafong hospital.



METHODS

This is a retrospective audit of HIV-infected children, initiated on ART between October 2003 and December 2007. This group of patients were subdivided into two groups according to outcome:

- **Group A:** Patients on ART currently alive;
- **Group B:** Patients on ART with death as the outcome (serious adverse event).

The data analyzed included the following: 1) demographic data, 2) nutritional data and 3) medical data. Currently only Group B has been analyzed fully in order to improve future treatment.

RESULTS

The mortality was 8.5% for the whole study population (53/621), which was 100% for Group B.

The patients in Group B were statistically significantly younger (2 years 1 month) than the patients in Group A (4 years) ($p=0.000$) with slightly more boys in Group B (see table 1).

Table 1: Demographic data of Groups A and B

	Group A (n=621)	Group B (n=53)
Mean age at initiation	4 years	2 years 1 month
Age range	3 weeks – 17 years 5 months	2 months – 12 years 9 months
Male to female ratio	1:1	1.3:1
Mean duration on ART at death	n/a	4 months
Range duration on ART at death	n/a	2 days – 1 year 11 months

HIV disease stage classification changed from the 3-stage to the 4-stage WHO classification from January 2006 onwards. For the purpose of this presentation the second period was analysed. Group B (75%) had more advanced disease than Group A (47%), although this was not statistically significant (see table 2).

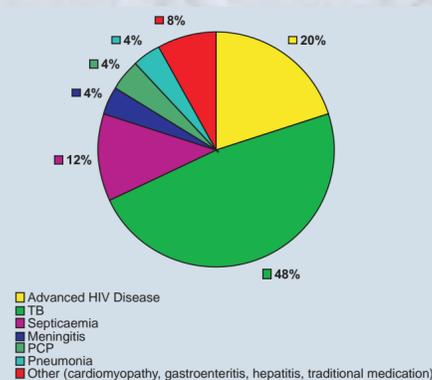
Co-morbid disease was another important finding in Group B patients, which included underweight, stunting, anaemia, encephalopathy and tuberculosis (see table 3).

The mean CD4 percentages were similar in both groups (12% in group A and 14% in group B, $p=0.33$), while CD4 percentage groupings are given in table 4. Detectable viral loads after 6 months of treatment were found in 24% of patients in Group B.

Mean duration of ART at death was 4 months (see table 1), with death occurring within 2 months of ART initiation in 56%, while 74% of children demised within 6 months of start of treatment. The most common cause of death was tuberculosis (48%), followed by advanced AIDS (20%) (see graph 1).

There were also significant social factors that impacted on outcome in Group B, including poor home environment, absent primary caregiver and poor family circumstances. Adherence problems (adherence < 95% or missed > 1 dose/day; missed appointments) were recorded in 50% of patient files.

Furthermore 25% of Group B patients were seen by junior doctors (interns) during follow-up visits that may have led to under-diagnosis of progression of disease or complications.



Graph 1: Primary cause of death in Group B (n=46)

Table 2: Percentage of children in WHO staging at ART initiation using 4-stage WHO staging system (Jan 2006 -Dec 2007)

	Group A% (n=324)	Group B% (n=16)
WHO Stage 1	2	0
WHO Stage 2	11	0
WHO Stage 3	40	25
WHO Stage 4	47	75

Table 3: Co-morbid disease at initiation in Group B patients

	=46 (n=52; #6 patient records incomplete)	%
Underweight (defined as mass < 80% of expected weight for age)		83
Stunting (defined as height < 90% expected height for age)		74
Anaemia *(n=33) (Hb<9); * data was missing for 13 patients		49
Encephalopathy (fulfillment of any of the following 3 criteria – delayed milestones; small for age skull circumference; brisk reflexes)		39
TB at ART initiation		48
TB throughout ART		65

Table 4: CD4-Percentages at ART initiation of Group A and Group B

	Group A% (n=552) (n=621 : #9 patient records incomplete)	Group B% (n=52)
CD4% <15%	40	40
CD4% 10% - 15%	26	21
CD4% <10%	34	39
Mean CD4%	12	14

CONCLUSIONS

- The overall mortality for HIV-infected children on ART was 8.5%.
- Tuberculosis was the major cause of death. Death as poor outcome was found in younger patients with probably rapid progressive disease.
- These patients had significant co-morbidity, as well as more than one social factor that potentially impacted negatively on the outcome, such a non-compliance.
- There was no difference in CD4% between the two groups.
- A quarter of the patients that died were seen by junior doctors, who may have under diagnosed complications or progression of disease.
- For the above mentioned findings we propose a risk stratification system to identify high risk children with AIDS who should receive specialized paediatric care and more regular visits, as well identification of low risk patients who can be down-referred to primary care clinics