Addison’s disease associated with advanced HIV may explain the high mortality

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# Table 1 : Patient profile text : 03-08-2022

The age median age at enrolment was 36 with the interquartile range IQR (31,41), with unusually equal male and female participation at 49.2% and 50.8%, repectively. Black Africans constituted the majority of the participants at 357(83.4%), compared to 68 (15.9%) mixed-race, and an insignificant number of Asians 1 (0.2%) and Caucasians 2 (0.5%). The duration of illness was 14 days with IQR (14, 21), and almost all the patients had opportunistic infections 424 (99.1%), which is consistent with the advanced nature of their disease as reflected by the admission criteria of the CD4 level of 100 or less. The Log viral load was 4.54 with the IQR (3.16, 5.35) and the CD4 count was a very low 31 with the IQR (14, 60). The overall sodium was slightly less than normal at 134 with IQR (130, 137.0), while potassium was normal at 4.10 with the IQR (3.6,4.6). Although the white cell count and the neutrophils were normal, the haemoglobin and the lymphocyte count and we are both low at 8.70 with the IQR 7.40,10,30) and 0.8 with the IQR (0.4,1.8), respectively. The PAI prevalence rate was 30 (9.4%).

# Table 1: Profile of patients

| Variable | N | N = 4311 |
| --- | --- | --- |
| **Age at enrolment** | 430 | 36 (31, 42) |
| **gender** | 429 |  |
| Females |  | 218 (50.8%) |
| Males |  | 211 (49.2%) |
| **Ethnicity** | 428 |  |
| Asian |  | 1 (0.2%) |
| Black African |  | 357 (83.4%) |
| Coloured |  | 68 (15.9%) |
| White |  | 2 (0.5%) |
| **Duration of current illness** | 400 | 14 (14, 21) |
| **Opportunistic infection present** | 428 | 424 (99.1%) |
| **log10 viral load** | 97 | 4.54 (3.16, 5.35) |
| **Total CD4 count** | 428 | 31 (14, 60) |
| **Sodium** | 408 | 134.0 (130.0, 137.0) |
| **Potassium** | 409 | 4.10 (3.60, 4.60) |
| **Haemoglobin** | 426 | 8.70 (7.40, 10.30) |
| **White cell count** | 423 | 5.3 (3.5, 8.0) |
| **Lymphocyte count** | 93 | 0.8 (0.4, 1.8) |
| **Neutrophils** | 93 | 3 (1, 8) |
| **Addisons disease** | 318 | 30 (9.4%) |
| 1Median (IQR); n (%) | | |

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# Tables 2, 3 & 4 in text:

Comparison between the PAI and the non-PAI patients revealed no significant differences in all the variables of interest. However, the bivariate analysis without imputed data revealed the Log viral-load which was associated with mortality as shown by the HR 1.57 with the CI 1.00, 2.47 and the significant p-value (*p* = 0.049). Bivariate analysis with imputed data confirms the Log viral-load association with mortality as reflected by the HR 1.51, the CI (1.22,187) and a very significant p-value (*p*< 0.001). It also reveals a reduction in the hazard of dying with every unit rise in neutrophils as reflected by the HR 0.98, CI (0.96, 0.99) and a significant p-value (*p*=0.010). Multivariate analysis revealed Log viral-load associated with increased mortality and a unit increase in neutrophils and lymphocytes associated with reduced hazard of dying with p-values of (*p*=0.007) and (*p*=0.009), respectively.

# Table 2: comparing Addisons status with other variables

| Variable | N | no, N = 2881 | yes, N = 301 | p-value2 |
| --- | --- | --- | --- | --- |
| **Age at enrolment** | 318 | 36 (31, 42) | 36 (31, 43) | 0.9 |
| **gender** | 318 |  |  | >0.9 |
| Females |  | 151 (52.4%) | 16 (53.3%) |  |
| Males |  | 137 (47.6%) | 14 (46.7%) |  |
| **Ethnicity** | 317 |  |  | 0.5 |
| Black African |  | 235 (81.9%) | 26 (86.7%) |  |
| Other |  | 52 (18.1%) | 4 (13.3%) |  |
| **Duration of current illness** | 300 | 14 (14, 30) | 14 (14, 21) | 0.4 |
| **Opportunistic infection present** | 317 |  |  |  |
| Yes |  | 287 (100.0%) | 30 (100.0%) |  |
| **log10 viral load** | 65 | 4.71 (3.27, 5.37) | 5.04 (4.79, 5.17) | 0.6 |
| **Total CD4 count** | 317 | 31 (14, 56) | 26 (12, 56) | 0.6 |
| **Sodium** | 303 | 133.0 (130.0, 137.0) | 135.0 (131.0, 137.0) | 0.10 |
| **Potassium** | 304 | 4.10 (3.65, 4.60) | 3.90 (3.30, 4.60) | 0.4 |
| **Haemoglobin** | 317 | 8.80 (7.40, 10.40) | 8.30 (7.62, 10.37) | >0.9 |
| **White cell count** | 316 | 5.7 (3.9, 8.2) | 5.1 (2.9, 8.2) | 0.5 |
| **Lymphocyte count** | 62 | 0.7 (0.4, 1.6) | 0.9 (0.6, 1.3) | 0.3 |
| **Neutrophils** | 61 | 3 (1, 7) | 7 (1, 15) | 0.7 |
| 1Median (IQR); n (%) | | | | |
| 2Wilcoxon rank sum test; Pearson's Chi-squared test | | | | |

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# Table 3: Bivariate table

| Characteristic | N | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- | --- |
| Age\_at\_enrolment | 430 | 1.02 | 0.99, 1.05 | 0.2 |
| gender | 429 | 0.78 | 0.45, 1.34 | 0.4 |
| Ethnicity | 428 | 0.89 | 0.42, 1.88 | 0.8 |
| Duration\_of\_current\_illness | 400 | 1.00 | 0.99, 1.01 | 0.6 |
| Log10\_viralload | 97 | 1.57 | 1.00, 2.47 | 0.049 |
| Total\_CD4\_count | 428 | 0.99 | 0.98, 1.00 | 0.2 |
| Sodium | 408 | 0.99 | 0.95, 1.04 | 0.7 |
| Potassium | 409 | 0.85 | 0.63, 1.15 | 0.3 |
| Haemoglobin | 426 | 1.00 | 0.97, 1.02 | 0.8 |
| White\_cell\_count | 423 | 1.00 | 1.00, 1.00 | 0.8 |
| Lymphocyte\_count | 93 | 0.86 | 0.68, 1.09 | 0.2 |
| Neutrophils | 93 | 0.99 | 0.96, 1.02 | 0.5 |
| Addisons\_disease | 318 | 1.18 | 0.47, 2.97 | 0.7 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | | |

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# Table 4: Multivariate table (generated with imputed data)

The rule of thumb for MV models such as this on you need at least 10 people per outcome. We have 53 people with the outcome, yet we have 6 variables adjusted for in the model (using stepwise regression). I suggest we remove one variable from the list that you think may not be biologically contributing in the relationship.

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | Adj.HR | 95%CI | P value |
| Addison's disease | 0.565 | (0.21813, 1.46569) | 0.240693729 |
| Log10 Viral load | 1.774 | (1.41225, 2.22899) | 8.44E-07 |
| Neutrophils | 0.974 | (0.95467, 0.99279) | 0.007263384 |
| Lymphocyte count | 0.924 | (0.87072, 0.98059) | 0.009145005 |
| Potassium | 0.862 | (0.65495, 1.13395) | 0.288136069 |