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

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# Table 1

| Variable | N | Overall, N = 4291 | Females, N = 2181 | Males, N = 2111 | p-value2 |
| --- | --- | --- | --- | --- | --- |
| **Age at enrolment** | 429 | 36 (31, 42) | 35 (31, 41) | 37 (32, 43) | 0.058 |
| **Ethnicity** | 427 |  |  |  | 0.069 |
| Asian |  | 1 (0.2%) | 0 (0.0%) | 1 (0.5%) |  |
| Black African |  | 356 (83.4%) | 176 (81.1%) | 180 (85.7%) |  |
| Coloured |  | 68 (15.9%) | 41 (18.9%) | 27 (12.9%) |  |
| White |  | 2 (0.5%) | 0 (0.0%) | 2 (1.0%) |  |
| **Duration of current illness** | 399 | 14 (14, 21) | 14 (14, 30) | 14 (14, 21) | 0.3 |
| **Opportunistic infection present** | 426 | 423 (99.3%) | 214 (98.6%) | 209 (100.0%) | 0.2 |
| **log10 viral load** | 96 | 4.47 (3.13, 5.34) | 4.07 (3.22, 5.24) | 4.61 (3.04, 5.37) | >0.9 |
| **Total CD4 count** | 427 | 31 (14, 60) | 32 (15, 58) | 30 (12, 64) | >0.9 |
| **Sodium** | 407 | 134.0 (130.0, 137.0) | 135.0 (131.0, 138.0) | 133.0 (129.0, 136.5) | 0.001 |
| **Potassium** | 408 | 4.05 (3.60, 4.60) | 3.90 (3.50, 4.40) | 4.20 (3.80, 4.70) | <0.001 |
| **Haemoglobin** | 425 | 8.70 (7.40, 10.30) | 8.30 (7.10, 9.50) | 9.30 (7.90, 10.90) | <0.001 |
| **White cell count** | 422 | 5.4 (3.6, 8.0) | 5.6 (3.7, 8.1) | 5.3 (3.5, 7.8) | 0.6 |
| **Lymphocyte count** | 92 | 0.8 (0.4, 1.8) | 0.9 (0.3, 3.5) | 0.8 (0.4, 1.3) | >0.9 |
| **Neutrophils** | 92 | 3 (1, 8) | 3 (1, 10) | 3 (1, 7) | 0.6 |
| **Addisons disease** | 318 | 21 (6.6%) | 10 (6.0%) | 11 (7.3%) | 0.6 |
| **Tuberculosis** | 429 |  |  |  | 0.7 |
| Checked |  | 313 (73.0%) | 161 (73.9%) | 152 (72.0%) |  |
| Unchecked |  | 116 (27.0%) | 57 (26.1%) | 59 (28.0%) |  |
| **Cryptococcus neoformans** | 429 |  |  |  | >0.9 |
| Checked |  | 1 (0.2%) | 1 (0.5%) | 0 (0.0%) |  |
| Unchecked |  | 428 (99.8%) | 217 (99.5%) | 211 (100.0%) |  |
| **Toxoplasmosis** | 429 |  |  |  |  |
| Unchecked |  | 429 (100.0%) | 218 (100.0%) | 211 (100.0%) |  |
| **Mycobacterium avium-intracellulare** | 429 |  |  |  |  |
| Unchecked |  | 429 (100.0%) | 218 (100.0%) | 211 (100.0%) |  |
| **Kaposis sarcoma** | 429 |  |  |  | 0.5 |
| Checked |  | 1 (0.2%) | 0 (0.0%) | 1 (0.5%) |  |
| Unchecked |  | 428 (99.8%) | 218 (100.0%) | 210 (99.5%) |  |
| **Cytomegalovirus** | 429 |  |  |  | 0.5 |
| Checked |  | 1 (0.2%) | 0 (0.0%) | 1 (0.5%) |  |
| Unchecked |  | 428 (99.8%) | 218 (100.0%) | 210 (99.5%) |  |
| **Other** | 429 |  |  |  | 0.5 |
| Checked |  | 113 (26.3%) | 54 (24.8%) | 59 (28.0%) |  |
| Unchecked |  | 316 (73.7%) | 164 (75.2%) | 152 (72.0%) |  |
| 1Median (IQR); n (%) | | | | | |
| 2Wilcoxon rank sum test; Fisher's exact test; Pearson's Chi-squared test | | | | | |

# Table 2: comparing Addisons status with other variables

| Variable | N | yes, N = 211 | no, N = 2971 | p-value2 |
| --- | --- | --- | --- | --- |
| **Age at enrolment, median (IQR) (years)** | 318 | 36 (31, 43) | 36 (31, 42) | 0.6 |
| **Gender, n(%)** | 318 |  |  | 0.6 |
| Females |  | 10 (47.6%) | 157 (52.9%) |  |
| Males |  | 11 (52.4%) | 140 (47.1%) |  |
| **Ethnicity, n(%)** | 317 |  |  | 0.6 |
| Black African |  | 19 (90.5%) | 242 (81.8%) |  |
| Other |  | 2 (9.5%) | 54 (18.2%) |  |
| **Duration of current illness, median (IQR) (days)** | 300 | 14 (11, 21) | 14 (14, 30) | 0.2 |
| **Random cortisol** | 318 | 332 (253, 375) | 513 (388, 606) | <0.001 |
| **Basal cortisol** | 144 | 300 (185, 328) | 462 (352, 568) | <0.001 |
| **Stimulated cortisol** | 145 | 403 (316, 438) | 720 (616, 848) | <0.001 |
| **ACTH** | 318 | 37 (25, 72) | 31 (18, 48) | 0.029 |
| **BP (systolic)** | 318 | 120 (111, 129) | 110 (100, 125) | 0.10 |
| **BP (diastolic)** | 318 | 71 (70, 80) | 70 (60, 78) | 0.031 |
| **Heart rate** | 318 | 90 (77, 109) | 95 (81, 111) | 0.5 |
| **Hypotension** | 305 | 1 (4.8%) | 22 (7.7%) | >0.9 |
| **Weakness** | 306 | 16 (76.2%) | 252 (88.4%) | 0.2 |
| **Tiredness** | 307 | 18 (85.7%) | 261 (91.3%) | 0.4 |
| **Poor appetite** | 304 | 18 (85.7%) | 226 (79.9%) | 0.8 |
| **Weight loss** | 308 | 18 (85.7%) | 264 (92.0%) | 0.4 |
| **Increased pigmentation of the skin** | 292 | 8 (44.4%) | 131 (47.8%) | 0.8 |
| **Nausea** | 307 | 12 (57.1%) | 151 (52.8%) | 0.7 |
| **Vomiting** | 306 | 6 (28.6%) | 82 (28.8%) | >0.9 |
| **Liking for salt** | 305 | 14 (66.7%) | 193 (68.0%) | >0.9 |
| **Hypoglycaemia** | 306 | 0 (0.0%) | 7 (2.5%) | >0.9 |
| **Loss of consciousness** | 304 | 0 (0.0%) | 2 (0.7%) | >0.9 |
| **Diarrhoea** | 304 | 6 (28.6%) | 121 (42.8%) | 0.2 |
| **Dizziness** | 305 | 11 (55.0%) | 133 (46.7%) | 0.5 |
| **Shock** | 308 | 0 (0.0%) | 3 (1.0%) | >0.9 |
| **Anorexia** | 306 | 7 (33.3%) | 126 (44.2%) | 0.3 |
| **Loss of axillary and pubic hair, if female** | 309 |  |  | 0.8 |
| No |  | 8 (38.1%) | 103 (35.8%) |  |
| Not applicable |  | 11 (52.4%) | 134 (46.5%) |  |
| Yes |  | 2 (9.5%) | 51 (17.7%) |  |
| **Any postural drop in blood pressure** | 306 | 1 (4.8%) | 11 (3.9%) | 0.6 |
| **Presence of anaemia** | 303 | 12 (57.1%) | 155 (55.0%) | 0.8 |
| **Presence of an opportunistic infection** | 317 |  |  |  |
| Yes |  | 21 (100.0%) | 296 (100.0%) |  |
| **Viral load (log10 Copies/mL)** | 65 | 4.79 (4.67, 4.92) | 4.77 (3.28, 5.36) | >0.9 |
| **Total CD4 count** | 317 | 23 (14, 48) | 31 (14, 57) | 0.6 |
| **Sodium mmol/L** | 303 | 135.0 (132.0, 137.0) | 133.0 (130.0, 137.0) | 0.12 |
| **Potassium mmol/L** | 304 | 3.70 (3.30, 4.00) | 4.20 (3.70, 4.60) | 0.045 |
| **Haemoglobin g/dL** | 317 | 8.40 (7.60, 10.30) | 8.80 (7.40, 10.40) | 0.9 |
| **White cell count X109** | 316 | 5.2 (2.5, 6.5) | 5.7 (3.9, 8.3) | 0.3 |
| **Lymphocyte count X109** | 62 | 1.0 (0.6, 9.4) | 0.7 (0.4, 1.5) | 0.3 |
| **Neutrophils** | 61 | 1 (1, 1) | 3 (1, 7) | 0.055 |
| 1Median (IQR); n (%) | | | | |
| 2Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test | | | | |

| Variable | N | yes, N = 101 | no, N = 1541 | p-value2 |
| --- | --- | --- | --- | --- |
| **Loss of axillary and pubic hair, if female** | 164 | 2 (20.0%) | 51 (33.1%) | 0.5 |
| 1n (%) | | | | |
| 2Fisher's exact test | | | | |

# Table 3: Bivariate table

# Table 3a: Deep dive on Addison’s disease patients

| Variable | N | yes, N = 5 | no, N = 42 | p-value |
| --- | --- | --- | --- | --- |
| **Age at enrolment median (IQR) (years)** | 47 | 40 (31, 41) | 38 (33, 44) | >0.9 |
| **Gender, n(%)** | 47 |  |  | >0.9 |
| Females |  | 3 (60.0%) | 25 (59.5%) |  |
| Males |  | 2 (40.0%) | 17 (40.5%) |  |
| **Ethnicity, n(%)** | 47 |  |  | >0.9 |
| 1 |  | 4 (80.0%) | 35 (83.3%) |  |
| 2 |  | 1 (20.0%) | 7 (16.7%) |  |
| **Duration of current illness, median (IQR) (days)** | 44 | 9 (7, 266) | 1,257 (340, 2,792) | 0.067 |
| **Random cortisol** | 47 | 332 (281, 337) | 508 (367, 623) | 0.019 |
| **Basal cortisol** | 26 | 315 (301, 381) | 485 (419, 631) | 0.002 |
| **Stimulated cortisol** | 26 | 403 (347, 431) | 763 (630, 880) | <0.001 |
| **ACTH** | 47 | 48 (37, 88) | 39 (22, 53) | 0.3 |
| **BP (systolic)** | 47 | 127 (120, 128) | 110 (102, 120) | 0.2 |
| **BP (diastolic)** | 47 | 71 (63, 76) | 72 (67, 80) | 0.5 |
| **Heart rate** | 47 | 92 (68, 100) | 91 (80, 108) | 0.4 |
| **Hypotension** | 46 | 0 (0.0%) | 5 (12.2%) | >0.9 |
| **Weakness** | 46 | 3 (60.0%) | 38 (92.7%) | 0.084 |
| **Tiredness** | 45 | 5 (100.0%) | 37 (92.5%) | >0.9 |
| **Poor appetite** | 46 | 5 (100.0%) | 38 (92.7%) | >0.9 |
| **Weight loss** | 46 | 4 (80.0%) | 36 (87.8%) | 0.5 |
| **Increased pigmentation of the skin** | 44 | 2 (50.0%) | 24 (60.0%) | >0.9 |
| **Nausea** | 46 | 4 (80.0%) | 27 (65.9%) | >0.9 |
| **Vomiting** | 46 | 2 (40.0%) | 11 (26.8%) | 0.6 |
| **Liking for salt** | 46 | 3 (60.0%) | 28 (68.3%) | >0.9 |
| **Hypoglycaemia** | 46 |  |  |  |
| No |  | 5 (100.0%) | 41 (100.0%) |  |
| **Loss of consciousness** | 46 | 0 (0.0%) | 1 (2.4%) | >0.9 |
| **Diarrhoea** | 46 | 0 (0.0%) | 23 (56.1%) | 0.049 |
| **Dizziness** | 45 | 3 (60.0%) | 25 (62.5%) | >0.9 |
| **Shock** | 46 | 0 (0.0%) | 1 (2.4%) | >0.9 |
| **Anorexia** | 46 | 2 (40.0%) | 24 (58.5%) | 0.6 |
| **Loss of axillary and pubic hair, if female** | 45 |  |  | 0.8 |
| No |  | 2 (40.0%) | 11 (27.5%) |  |
| Not applicable |  | 2 (40.0%) | 15 (37.5%) |  |
| Yes |  | 1 (20.0%) | 14 (35.0%) |  |
| **Any postural drop in blood pressure** | 45 | 0 (0.0%) | 2 (5.0%) | >0.9 |
| **Presence of anaemia** | 46 | 3 (60.0%) | 24 (58.5%) | >0.9 |
| **Presence of an opportunistic infection** | 47 |  |  |  |
| Yes |  | 5 (100.0%) | 42 (100.0%) |  |
| **Tuberculosis** | 47 |  |  | 0.6 |
| Checked |  | 3 (60.0%) | 29 (69.0%) |  |
| Unchecked |  | 2 (40.0%) | 13 (31.0%) |  |
| **Cryptococcus neoformans** | 47 |  |  | >0.9 |
| Checked |  | 0 (0.0%) | 0 (0.0%) |  |
| Unchecked |  | 5 (100.0%) | 42 (100.0%) |  |
| **Toxoplasmosis** | 47 |  |  |  |
| Unchecked |  | 5 (100.0%) | 42 (100.0%) |  |
| **Mycobacterium avium-intracellulare** | 47 |  |  |  |
| Unchecked |  | 5 (100.0%) | 42 (100.0%) |  |
| **Kaposis sarcoma** | 47 |  |  | >0.9 |
| Checked |  | 0 (0.0%) | 0 (0.0%) |  |
| Unchecked |  | 5 (100.0%) | 42 (100.0%) |  |
| **Cytomegalovirus** | 47 |  |  | >0.9 |
| Checked |  | 0 (0.0%) | 0 (0.0%) |  |
| Unchecked |  | 5 (100.0%) | 42 (100.0%) |  |
| **Other** | 47 |  |  | >0.9 |
| Checked |  | 2 (40.0%) | 14 (33.3%) |  |
| Unchecked |  | 3 (60.0%) | 28 (66.7%) |  |
| **Viral load (log10 Copies/mL)** | 11 | NA (NA, NA) | 5.10 (4.55, 5.68) |  |
| **Total CD4 count** | 47 | 17 (15, 46) | 28 (14, 49) | 0.9 |
| **Sodium mmol/L** | 45 | 134.0 (133.0, 139.0) | 133.0 (128.0, 137.0) | 0.3 |
| **Potassium mmol/L** | 45 | 3.60 (3.30, 3.90) | 3.90 (3.60, 4.52) | 0.14 |
| **Haemoglobin g/dL** | 47 | 8.70 (8.10, 10.50) | 8.85 (7.50, 10.70) | >0.9 |
| **White cell count X109** | 47 | 5.8 (3.9, 10.8) | 5.4 (3.9, 7.7) | 0.7 |
| **Lymphocyte count X109** | 12 | NA (NA, NA) | 0.72 (0.38, 1.07) |  |

# Table 3b: Deep dive in mortality status among Addissons cases

| Variable | N | yes, N = 5 | no, N = 16 | p-value |
| --- | --- | --- | --- | --- |
| **Age at enrolment median (IQR) (years)** | 21 | 40 (31, 41) | 36 (32, 44) | >0.9 |
| **Gender, n(%)** | 21 |  |  | 0.6 |
| Females |  | 3 (60.0%) | 7 (43.8%) |  |
| Males |  | 2 (40.0%) | 9 (56.2%) |  |
| **Ethnicity, n(%)** | 21 |  |  | 0.4 |
| 1 |  | 4 (80.0%) | 15 (93.8%) |  |
| 2 |  | 1 (20.0%) | 1 (6.2%) |  |
| **Duration of current illness, median (IQR) (days)** | 20 | 9 (7, 266) | 1,812 (346, 3,326) | 0.12 |
| **Random cortisol** | 21 | 332 (281, 337) | 298 (230, 376) | 0.8 |
| **Basal cortisol** | 21 | 315 (301, 381) | 275 (180, 326) | 0.2 |
| **Stimulated cortisol** | 21 | 403 (347, 431) | 398 (312, 447) | >0.9 |
| **ACTH** | 21 | 48 (37, 88) | 32 (25, 72) | 0.5 |
| **BP (systolic)** | 21 | 127 (120, 128) | 120 (110, 130) | 0.9 |
| **BP (diastolic)** | 21 | 71 (63, 76) | 74 (70, 85) | 0.3 |
| **Heart rate** | 21 | 92 (68, 100) | 87 (79, 115) | 0.5 |
| **Hypotension** | 21 | 0 (0.0%) | 1 (6.2%) | >0.9 |
| **Weakness** | 21 | 3 (60.0%) | 13 (81.2%) | 0.6 |
| **Tiredness** | 21 | 5 (100.0%) | 13 (81.2%) | 0.5 |
| **Poor appetite** | 21 | 5 (100.0%) | 13 (81.2%) | 0.5 |
| **Weight loss** | 21 | 4 (80.0%) | 14 (87.5%) | >0.9 |
| **Increased pigmentation of the skin** | 18 | 2 (50.0%) | 6 (42.9%) | >0.9 |
| **Nausea** | 21 | 4 (80.0%) | 8 (50.0%) | 0.3 |
| **Vomiting** | 21 | 2 (40.0%) | 4 (25.0%) | 0.6 |
| **Liking for salt** | 21 | 3 (60.0%) | 11 (68.8%) | >0.9 |
| **Hypoglycaemia** | 21 |  |  |  |
| No |  | 5 (100.0%) | 16 (100.0%) |  |
| **Loss of consciousness** | 20 |  |  |  |
| No |  | 5 (100.0%) | 15 (100.0%) |  |
| **Diarrhoea** | 21 | 0 (0.0%) | 6 (37.5%) | 0.3 |
| **Dizziness** | 20 | 3 (60.0%) | 8 (53.3%) | >0.9 |
| **Shock** | 21 |  |  |  |
| No |  | 5 (100.0%) | 16 (100.0%) |  |
| **Anorexia** | 21 | 2 (40.0%) | 5 (31.2%) | >0.9 |
| **Loss of axillary and pubic hair, if female** | 21 |  |  | 0.8 |
| No |  | 2 (40.0%) | 6 (37.5%) |  |
| Not applicable |  | 2 (40.0%) | 9 (56.2%) |  |
| Yes |  | 1 (20.0%) | 1 (6.2%) |  |
| **Any postural drop in blood pressure** | 21 | 0 (0.0%) | 1 (6.2%) | >0.9 |
| **Presence of anaemia** | 21 | 3 (60.0%) | 9 (56.2%) | >0.9 |
| **Presence of an opportunistic infection** | 21 |  |  |  |
| Yes |  | 5 (100.0%) | 16 (100.0%) |  |
| **Tuberculosis** | 21 |  |  | >0.9 |
| Checked |  | 3 (60.0%) | 8 (50.0%) |  |
| Unchecked |  | 2 (40.0%) | 8 (50.0%) |  |
| **Cryptococcus neoformans** | 21 |  |  | >0.9 |
| Checked |  | 0 (0.0%) | 0 (0.0%) |  |
| Unchecked |  | 5 (100.0%) | 16 (100.0%) |  |
| **Toxoplasmosis** | 21 |  |  |  |
| Unchecked |  | 5 (100.0%) | 16 (100.0%) |  |
| **Mycobacterium avium-intracellulare** | 21 |  |  |  |
| Unchecked |  | 5 (100.0%) | 16 (100.0%) |  |
| **Kaposis sarcoma** | 21 |  |  | >0.9 |
| Checked |  | 0 (0.0%) | 0 (0.0%) |  |
| Unchecked |  | 5 (100.0%) | 16 (100.0%) |  |
| **Cytomegalovirus** | 21 |  |  | >0.9 |
| Checked |  | 0 (0.0%) | 1 (6.2%) |  |
| Unchecked |  | 5 (100.0%) | 15 (93.8%) |  |
| **Other** | 21 |  |  | >0.9 |
| Checked |  | 2 (40.0%) | 8 (50.0%) |  |
| Unchecked |  | 3 (60.0%) | 8 (50.0%) |  |
| **Viral load (log10 Copies/mL)** | 2 |  |  | >0.9 |
| 4.54181629404385 |  | 0 (NA%) | 1 (50.0%) |  |
| 5.04006012250337 |  | 0 (NA%) | 1 (50.0%) |  |
| **Total CD4 count** | 21 | 17 (15, 46) | 26 (13, 50) | >0.9 |
| **Sodium mmol/L** | 21 | 134.0 (133.0, 139.0) | 135.0 (131.8, 137.0) | 0.9 |
| **Potassium mmol/L** | 21 | 3.60 (3.30, 3.90) | 3.80 (3.27, 4.60) | 0.6 |
| **Haemoglobin g/dL** | 21 | 8.70 (8.10, 10.50) | 8.20 (7.57, 10.22) | 0.6 |
| **White cell count X109** | 21 | 6 (4, 11) | 4 (2, 6) | 0.3 |
| **Lymphocyte count X109** | 4 |  |  | >0.9 |
| 0.49000001 |  | 0 (NA%) | 1 (25.0%) |  |
| 0.600000024 |  | 0 (NA%) | 1 (25.0%) |  |
| 1.309999943 |  | 0 (NA%) | 1 (25.0%) |  |
| 33.59999847 |  | 0 (NA%) | 1 (25.0%) |  |
| **Addisons disease** | 21 | 5 (100.0%) | 16 (100.0%) | >0.9 |

# Table 4: Multivariate table

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. (see accompanying file)