**The effect of antiretroviral therapy and CD4 count on markers of infectiousness in HIV-associated tuberculosis**

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Supplemental Digital Content

**Figure legend**

**Figure S1**

Inclusions and exclusions for analysis, using the complete dataset from Thibela TB

**Tables**

**Table S1**: Univariable and multivariable analysis of associations between exposure variables and smear positivity

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Category of variable (number with known sputum smear status)** | | **Number in group**  **(% of group – column %)** | **Smear positive**  **n (% of category – row %)** | | **Unadjusted prevalence ratio (95% CI)** | **p-value (Wald test)** |
| **Univariable analysis** | |  |  | |  |  |
| Gender (n=1104) | | |  | |  |  |
|  | Male | 1071 (97.0) | 579 (54.1) | | 1.0 | 0.68 |
|  | Female | 33 (3.0) | 19 (57.6) | | 1.07 (0.79-1.43) |  |
| Age group (years) (n=900) | | |  | |  |  |
|  | <38 | 217 (24.1) | 117 (53.9) | | 1.0 | 0.38 |
|  | 38-42 | 211 (23.4) | 115 (54.5) | | 1.01 (0.85-1.20) |
|  | 43-47 | 223 (24.8) | 122 (54.7) | | 1.01 (0.85-1.20) |
|  | >47 | 249 (27.7) | 151 (60.6) | | 1.12 (0.96-1.32) |
| Episode type (n=1087) | | |  | |  |  |
|  | New episode | 723 (66.5) | 378 (52.3) | | 1.0 | 0.12 |
|  | Retreatment episode | 364 (33.5) | 208 (57.1) | | 1.09 (0.98-1.22) |
| Reported site of disease (n=1066) | | |  | |  |  |
|  | Pulmonary only | 738 (69.2) | 496 (67.2) | | 1.0 | <0.001 |
|  | Extrapulmonary only | 141 (13.2) | 17 (12.1) | | 0.18 (0.11-0.28) |
|  | Pulmonary and extrapulmonary | 50 (4.7) | 20 (40.0) | | 0.60 (0.42-0.84) |
|  | Miliary/disseminated | 137 (12.9) | 38 (27.7) | | 0.41 (0.31-0.54) |
| HIV status (n=1106)1 | | |  | |  |  |
|  | Negative | 285 (25.8) | 186 (65.3) | | 1.0 | <0.001 |
|  | Positive | 821 (74.2) | 413 (50.3) | | 0.77 (0.69-0.86) |
| CD4 count for HIV+ (cells/µL) (n=598) | | |  | |  |  |
|  | <100 | 199 (33.3) | 110 (55.3) | | 1.0 | 0.03 |
|  | 100-199 | 179 (29.9) | 74 (41.3) | | 0.75 (0.60-0.93) |
|  | 200-349 | 148 (24.7) | 69 (46.6) | | 0.84 (0.68-1.04) |
|  | >349 | 72 (12.0) | 30 (41.7) | | 0.75 (0.56-1.02) |
| cART status for HIV+ (n=749) | | | | |  |  |
|  | Not on cART | 515 (68.8) | | 267 (51.8) | 1.0 | 0.72 |
|  | On cART >90 days | 234 (31.2) | | 118 (50.4) | 0.97 (0.84-1.13) |
| Number of sputum specimens sent within 90 days before treatment start (n=1106) | | | | | | |
|  | One | 260 (23.5) | | 120 (46.2) | 1.0 | 0.003 |
|  | Two | 277 (25.1) | | 147 (53.1) | 1.15 (0.97-1.37) |
|  | Three | 273 (24.7) | | 170 (62.3) | 1.35 (1.15-1.58) |
|  | Four or more | 296 (26.8) | | 162 (54.7) | 1.19 (1.00-1.40) |
|  |  |  | |  |  |  |
|  |  |  | |  |  |  |
| **Multivariable analysis** | | | | |  |  |
| **Model (exposures)** | | **Number of episodes included** | | **Prevalence ratio (95% CI) smear positivity: cART >90 days vs. no cART** | | **p-value (Wald test)** |
|  | |  | |  |  |  |
| cART status only (unadjusted) | | 749 | | 0.97 (0.84-1.13) | | 0.72 |
| cART status only (restricted to episodes with all data available for multivariable model) | | 541 | | 0.92 (0.75-1.12) | | 0.39 |
| cART status, adjusted for episode type | | 541 | | 0.87 (0.71-1.07) | | 0.18 |
| cART status, adjusted for episode type and CD4 count | | 541 | | 0.89 (0.72-1.10) | | 0.28 |
| cART status, adjusted for episode type, CD4 count, number of sputa examined | | 541 | | 0.90 (0.73-1.11) | | 0.34 |

1Comparing HIV-positive on cART for >90 days versus baseline group HIV-positive not on cART

PR = prevalence ratio

**Table S2:** Radiological features of pulmonary tuberculosis, by HIV and cART status, for 495 individuals included in analysis of chest radiographs

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Radiological abnormality described | | Number (%) with abnormality, by HIV and cART status  n(%) of total given, unless otherwise specified | | | | |
| HIV+ not on cART  (n=224) | HIV+ on cART <=90 days  (n=28) | HIV+ on cART >90 days  (n=87) | HIV negative  (n=156) | total  (n= 495) |
| Abnormalities consistent with active tuberculosis1 | | 200 (89.3) | 27 (96.4) | 79 (90.8) | 147 (94.2) | 453 (91.5) |
| Cavitation2 | | 64 (28.6) | 10 (35.7) | 37 (42.5) | 109 (69.9) | 220 (44.4) |
|  | Cavitation >=4cm in total | 20 (8.9) | 3 (10.7) | 11 (12.6) | 32 (20.5) | 66 (13.3) |
| Fibrosis | | 50 (22.3) | 11 (39.3) | 25 (28.7) | 70 (44.9) | 156 (31.6) |
| Infiltrates | | 191 (85.3) | 28 (100) | 73 (83.9) | 146 (93.6) | 438 (88.5) |
| Miliary disease | | 6 (2.7) | 0 | 5 (5.8) | 7 (4.5) | 18 (3.6) |
| TB-related nodules or irregular opacities | | 27 (12.1) | 4 (14.3) | 10 (11.5) | 57 (36.5) | 98 (19.8) |
| Pleural effusion | | 33 (14.7) | 7 (25.0) | 15 (17.2) | 13 (8.3) | 68 (13.7) |
| Hilar or mediastinal lymphadenopathy | | 114 (50.9) | 14 (50.0) | 35 (40.2) | 65 (41.7) | 228 (46.1) |
| Non-calcified pericardial effusion | | 4 (1.8) | 0 | 1 (1.2) | 0 | 5 (1.0) |
| Calcified pericardial effusion | | 5 (2.2) | 0 | 0 | 1 (0.6) | 6 (1.2) |
| Silicosis at grade 1/1 or above | | 1/209  (7.7) | 1/23  (4.3) | 4/79  (5.1) | 10/101 (9.9) | 31/412  (7.5) |

1Abnormalities consistent with active tuberculosis in opinion of investigator reading the chest radiographs

2chi-squared p<0.001 for proportions with cavitation by study group

**Table S3**: Univariable and multivariable analysis of the effect of exposure variables on lung cavitation

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Category of variable (number with data and radiograph available)** | | **Number in group (% of group)** | **Cavitation**  **(% of group)** | **Unadjusted prevalence ratio (95% CI)** | **p-value (Wald test)** |
| Gender (n=494) | | |  |  |  |
|  | Male | 481 (97.4) | 216 (44.9) | 1 | 0.37 |
|  | Female | 13 (2.6) | 4 (30.8) | 0.69 (0.30-1.56) |  |
|  |  |  |  |  |  |
| Age group (years) (n=466) | | |  |  |  |
|  | <38 | 107 (23.0) | 42 (39.2) | 1 | 0.04 |
|  | 38-42 | 109 (23.4) | 44 (40.4) | 1.03 (0.74-1.43) |  |
|  | 43-47 | 118 (25.3) | 50 (42.4) | 1.08 (0.79-1.48) |  |
|  | >47 | 132 (28.3) | 72 (54.6) | 1.39 (1.05-1.84) |  |
|  | | | | |  |
| Episode type (n=487) | | |  |  |  |
|  | First episode | 319 (65.3) | 134 (42.1) | 1 | 0.13 |
|  | Subsequent episode | 169 (34.7) | 83 (49.1) | 1.17 (0.95-1.42) |  |
|  |  |  |  |  |  |
| HIV status (n=495) | | |  |  |  |
|  | Negative | 156 (31.5) | 109 (69.9) | 1 | <0.001 |
|  | Positive | 339 (68.5) | 111 (32.7) | 0.47 (0.39-0.56) |  |
|  |  |  |  |  |  |
| CD4 count for HIV+ (cells/µL) (n=281) | | |  |  |  |
|  | <100 | 93 (33.1) | 19 (20.4) | 1 | <0.001 |
|  | 100-199 | 85 (30.3) | 24 (29.2) | 1.38 (0.82-2.34) |  |
|  | 200-349 | 71 (25.3) | 26 (36.6) | 1.79 (1.08-2.97) |  |
|  | >349 | 32 (11.4) | 19 (59.4) | 2.91 (1.78-4.76) |  |
|  |  |  |  |  |  |
| cART status for HIV+ (n=311) | | | |  |  |
|  | Not on cART | 224 (72.0) | 64 (28.6) | 1 | 0.02 |
|  | On cART >90 days | 87 (28.0) | 37 (42.5) | 1.49 (1.08-2.05) |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
| **Multivariable analysis** | |  |  |  |  |
| **Model** | | **Number of episodes included** | **Prevalence ratio (95% CI) for cavitation: cART >90 days vs. no cART** | | **p-value (Wald test)** |
| cART status only (unadjusted) | | 311 | 1.49 (1.08 – 2.05) | | 0.02 |
| cART status only (restricted to episodes with all data available for multivariable analysis) | | 254 | 1.47 (1.01-2.14) | | 0.04 |
| cART status, adjusted for CD4 count | | 254 | 1.32 (0.90 – 1.92) | | 0.15 |
| cART status, adjusted for CD4 count and episode type | | 254 | 1.17 (0.80-1.71) | | 0.41 |

PR = prevalence ratio