**Table 1**. Clinical and demographic information of study participants.

|  |  |  |
| --- | --- | --- |
|  | All Pulmonary TB | non TB |
| Number of participants n, (%) | 322 106(33) | 216(67) |
| Male/Female ratio n, (%) | 168(52)/154(48) 67(63)/39(37) | 97(45)/119(55) |
| HIV status (pos/neg) n, (%) | 54(17)/268(83) 24(23)/82(77) | 30(14)/186(86) |
| QFT-IT result available n, (%) | 211(66) 78(37) | 133(63) |
| QFT-IT positive, n (%) | 111(53) 56(50) | 55(50) |
|  |  |  |

Abbreviation: QFT-IT = Quantiferon TB Gold In Tube; n = number

**Table 2.** Diagnostic potential of markers detected in overnight culture supernatant for TB disease

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Marker/WBA | Median TB | Median non TB | P value | AUC | Optimal cut off | Sensitivity  % | Specificity  % |
| CRPNil | 115296 (990-268405) | 4903 (0-268405) | 0.01 | 0.85 | 183 | 80 | 80 |
| SAA Nil | 1577 000 (0-1577000) | 4171 (0-1577000) | 0.01 | 0.79 | 166 | 81 | 72 |
| Ferritin Nil | 184000 (5668-495381) | 84602 (27.74-495381) | 0.01 | 0.74 | 172 | 70 | 70 |
| IP-10 Nil | 1984 (58.88-3889) | 618 (0-3889) | 0.01 | 0.77 | 170 | 77 | 71 |
| IL-6 Nil | 180.7 (0-1659) | 81.7 (0-1659) | 0.03 | 0.57 | 120 | 69 | 51 |
| IL-7 Nil | 9.44 (0-47.57) | 6.04 (0-47.57) | 0.01 | 0.60 | 114 | 55 | 63 |
| IL-9 Nil | 39.97 (0-128.2) | 31.87 (0-128.2) | 0.02 | 0.42 | 147 | 46 | 46 |
| IL-13 Nil | 6.65 (0-20.06) | 2.99 (0-20.06) | 0.01 | 0.39 | 50 | 45 | 42 |
| IFN-γ Nil | 121.6 (0-396.1) | 85.3 (0-396.1) | 0.01 | 0.59 | 127 | 58 | 60 |
| VEGF Nil | 157.5 (4.1-455.9) | 107.5 (0-455.9 | 0.01 | 0.60 | 134 | 66 | 50 |
| Haptoglobin Nil | 92400000 (33178-92400000) | 2340000 (0-92400000) | 0.01 | 0.61 | 158 | 64 | 59 |
| SAP Nil | 112884 (15819-381489) | 83860 (0-381489) | 0.01 | 0.59 | 172 | 53 | 62 |
| PCT Nil | 8785 (1567-15324) | 8184 (1567-15324) | 0.03 | 0.43 | 160 | 39 | 58 |
| IP-10 Ag-Nil | 3943 (0-20816) | 1781 (0-20816) | 0.01 | 0.64 | 174 | 60 | 65 |
| IFN-γ Ag-Nil | 347.7 (0-1346) | 145.5 (0-1346) | 0.01 | 0.64 | 178 | 57 | 70 |
| IL-1ra Ag-Nil | 633.7 (0-2845) | 415.2 (0-2845) | 0.01 | 0.59 | 157 | 59 | 56 |
| tPA Ag-Nil | 301.6 (0-3908) | 0.0 (0-3908) | 0.01 | 0.58 | 167 | 55 | 61 |
| TRAIL Ag-Nil | 12.64 (0-144.0) | 0.0 (0-144.0) | 0.01 | 0.59 | 135 | 57 | 67 |
| IL-2 Rv1284-Nil | 3.30 (0-60.71) | 9.34 (0-60.71) | 0.03 | 0.58 | 151 | 52 | 67 |
| tPA Rv0081-Nil | 270.1 (0-3699) | 0.0 (0-3699) | 0.04 | 0.57 | 148 | 58 | 56 |
| IL-2 Rv2034-Nil | 0.0 (0-52.91) | 5.46 (0-52.91) | 0.01 | 0.60 | 96 | 69 | 52 |
| IL-17 Rv2034-Nil | 12.42 (0-213.4) | 26.3 (0-213.4) | 0.03 | 0.58 | 145 | 59 | 59 |
| FGF basic Rv2034-Nil | 4.35 (0-129.7) | 15.51 (0-129.7) | 0.03 | 0.58 | 166 | 50 | 64 |
| Ferritin Rv2034-Nil | 7624 (0-110159) | 521.5 (0-110159) | 0.02 | 0.58 | 184 | 52 | 66 |

Median levels of analytes (pg/ml) excluding SAA (ng/ml) and ranges (in parenthesis) showing accuracies in discriminating between active TB and non TB in overnight culture supernatants from all study participants. All analytes that showed significant differences (p<0.05) between the TB and non TB cases according to the Mann Whitney U test are shown. Optimal cut off values, sensitivity and specificity were selected based on Youden’s index. The levels of the different antigens shown were corrected for background subtraction of the unstimulated levels. AUC= Area under the receiver operator characteristics curve, Nil= unstimulated marker levels and Ag= ESAT-6/CFP-10 stimulated marker levels.

**Table 3.** Diagnostic potential of markers detected in overnight culture supernatants in discriminating LTBI from uninfected controls

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Marker/WBA | Median LTBI | Median non TB | P value | AUC | Optimal cut off | Sensitivity  % | Specificity  % |
| IL-1β Nil | 2.37 (0-70.54) | 6.64 (0-70.54) | 0.01 | 0.65 | 3.9 | 64 | 67 |
| IL-1Rα Nil | 159.9 (0-2005) | 399.0 (0-2005) | 0.01 | 0.62 | 140.3 | 75 | 49 |
| IL-2 Nil | 6.16 (0-80.04) | 13.22 (0-80.04) | 0.01 | 0.62 | 6.2 | 70 | 52 |
| IL-6 Nil | 19.17 (0-1653) | 116.4 (0-1653) | 0.01 | 0.68 | 51.8 | 66 | 74 |
| IL-10 Nil | 14.20 (0-150.2) | 27.01 (0-150.2) | 0.01 | 0.62 | 26.0 | 52 | 78 |
| MIP-1α Nil | 5.28 (0-89.85) | 11.15 (0-89.85) | 0.01 | 0.61 | 5.5 | 70 | 54 |
| TNF-α Nil | 21.32 (0-198.5) | 32.15 (0-198.5) | 0.01 | 0.63 | 29.5 | 56 | 70 |
| Eotaxin-2 Nil | 484.3 (28.42-1451) | 328.1 (0-1451) | 0.01 | 0.61 | 531.4 | 76 | 49 |
| IP-10 Ag-Nil | 5781 (0-20286) | 700 (0-20286) | 0.01 | 0.77 | 2669 | 75 | 72 |
| IFN-γ Ag-Nil | 376.3 (0-1189) | 106.1 (0-1189) | 0.01 | 0.76 | 196.7 | 71 | 74 |
| IL-1Rα Ag-Nil | 790.0 (0-2614) | 323.6 (0-2946) | 0.01 | 0.66 | 809.7 | 78 | 49 |
| GM-CSF Ag-Nil | 49.39 (0-168.0) | 21.51 (0-168.0) | 0.01 | 0.70 | 32.1 | 66 | 70 |
| MCP-1 Ag-Nil | 4653000 (0-4653000) | 27752 (0-4653000) | 0.01 | 0.66 | 781534 | 75 | 56 |
| MIP-1α Ag-Nil | 281.1 (0-1277) | 83.47 (0-1277) | 0.01 | 0.64 | 151.5 | 57 | 67 |
| IL-2 Ag-Nil | 173.8 (0-357.2) | 21.30 (0-357.2) | 0.01 | 0.80 | 74.8 | 77 | 69 |
| IL-4 Ag-Nil | 2.26 (0-6.52) | 1.04 (0-6.82) | 0.01 | 0.64 | 2.1 | 70 | 56 |
| IL-5 Ag-Nil | 5.72 (0-14.4) | 0 (0-14.4) | 0.01 | 0.68 | 5.7 | 86 | 50 |
| IL-13 Ag-Nil | 22.55 (0-56.09) | 2.50 (0-56.09) | 0.01 | 0.76 | 7.6 | 71 | 72 |
| IL-15 Ag-Nil | 95.74 (0-269.8) | 41.06 (0-269.8) | 0.01 | 0.63 | 78.5 | 67 | 60 |
| FGF basic Ag-Nil | 41.03 (0-137.3) | 21.31 (0-137.3) | 0.01 | 0.63 | 40.9 | 76 | 50 |
| Eotaxin-2 Ag-Nil | 76.15 (0-757.6) | 4.27 (0-757.6) | 0.01 | 0.63 | 252.5 | 88 | 38 |
| IL-8 Rv2034-Nil | 4075 (0-25911) | 2467 (0-25911) | 0.02 | 0.59 | 6111 | 71 | 46 |
| IL-15 Rv2034-Nil | 46.36 (0-245.7) | 27.42 (0-245.7) | 0.03 | 0.59 | 16.5 | 46 | 72 |
| MCP-1 Rv2034-Nil | 30946 (0-178009) | 5909 (0-178009) | 0.01 | 0.63 | 109303 | 85 | 40 |
| MIP-1α Rv2034-Nil | 58.69 (0-391.8) | 21.13 (0-391.8) | 0.02 | 0.60 | 1.8 | 34 | 87 |
| G-CSF Rv1284-Nil | 60.89 (0-343.5) | 30.07 (0-343.5) | 0.01 | 0.64 | 13.6 | 45 | 79 |
| MCP-1 Rv1284-Nil | 91386 (0-608346) | 17736 (0-608346) | 0.01 | 0.63 | 46586 | 69 | 57 |
| PDGF-BB Rv1284-Nil | 88.76 (0-740.5) | 0 (0-740.5) | 0.01 | 0.62 | 144.3 | 82 | 44 |

Median levels of analytes (pg/ml) and ranges (in parenthesis) showing accuracies in discriminating between LTBI and uninfected controls in overnight culture supernatants of all study participants. All analytes that showed significant differences (p<0.05) between LTBI and uninfected controls according to Mann Whitney U test are shown. Optimal cut off values, sensitivity and specificity were selected based on Youden’s index. The levels of the different antigens shown were corrected for background subtraction of the unstimulated levels. AUC= Area under the receiver operator characteristics curve, Nil= unstimulated marker levels and Ag= ESAT-6/CFP-10 stimulated marker level.

**Table 4.** Utility of combination of analytes in overnight culture supernatant in the diagnosis of TB

|  |  |  |  |
| --- | --- | --- | --- |
| Host marker model | Training classification set |  | Test classification set |
| 6 analyte model  All cases | **Non TB % TB %** | **Total %** | **Non TB % TB % Total %** |
| IP-10 Ag-Nil, IFN-γ Ag-Nil, IP-10Nil  Ferritin Nil, SAA Nil, CRP Nil | 84 77 | 82 | 78 83 80 |
| 6 analyte model  HIV uninfected | **Non TB % TB %** | **Total %** | **Non TB % TB % Total %** |
| IP-10 Ag-Nil, IFN-γ Ag-Nil, IP-10Nil  Ferritin Nil, SAA Nil, CRP Nil | 90 83 | 88 | 82 88 84 |
| 6 analyte model  HIV infected | **Resubstitution classification matrix** | | **Leave-one-out cross validation** |
|  | **Non TB % TB %** | **Total %** | **Non TB % TB %** |
| IP-10 Ag-Nil, IFN-γ Ag-Nil, IP-10Nil  Ferritin Nil, SAA Nil, CRP Nil | 80 64 | 73 | 76 52 |

Six analyte models generated by general discriminant analysis. Nil=unstimulated, Ag=ESAT-6/CFP-10