**Table S1** Percentages of measurements below the lower LOD for the 12 cytokines

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Total** | **Admission** | **Discharge** | **30-day** | **60-day** | **90-day** | **120-day** |
| **TNF-α, %** | 0.4 | 1.1 | 0 | 0 | 0 | 0 | 0 |
| **INF-γ, %** | 23.5 | 47.1 | 10.2 | 5.3 | 0 | 5.3 | 17.6 |
| **IL-2, %** | 37.6 | 31.0 | 40.9 | 42.1 | 22.2 | 36.8 | 58.8 |
| **IL-4, %** | 7.3 | 8.0 | 9.1 | 5.3 | 11.1 | 0 | 5.9 |
| **IL-5, %** | 1.7 | 3.4 | 1.1 | 0 | 0 | 0 | 0 |
| **IL-17E, %** | 2.6 | 0 | 6.8 | 0 | 0 | 0 | 0 |
| **IL-6, %** | 0.4 | 1.1 | 0 | 0 | 0 | 0 | 0 |
| **IL-17A, %** | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **IL-21, %** | 29.5 | 42.5 | 20.5 | 15.8 | 11.1 | 26.3 | 35.3 |
| **IL-22, %** | 15.4 | 6.9 | 29.5 | 10.5 | 0 | 10.5 | 0 |
| **IL-23, %** | 0.9 | 1.1 | 2.3 | 0 | 0 | 0 | 0 |
| **IL-10, %** | 28.6 | 32.2 | 27.3 | 21.1 | 11.1 | 21.1 | 41.2 |

**Abbreviations:** LOD, limit of detection; TNF, tumor necrosis factor; INF, interferon; IL, interleukin.

**Table S2** Levels of cytokines at admission of the patients in the three clusters

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Cluster 1**  **(n = 26)** | **Cluster 2**  **(n = 56)** | **Cluster 3**  **(n = 5)** | ***p*-value** |
| **TNF-α, pg/ml** | 70.06 (32.16-207.88) | 26.24(17.06-83.67) | 679.6(126.77-6410.50) | <0.001\*\*,†† |
| **IL-4, pg/ml** | 117.69(66.89-153.73) | 45.92(19.49-73.27) | 57.33(49.81-84.35) | <0.001\*\*\* |
| **IL-5, pg/ml** | 20.49(2.98-26.19) | 7.5(2.74-16.08) | 10.33(3.42-57.70) | 0.098 |
| **IL-17E, pg/ml** | 869.26(729.77-1417.00) | 253.11(175.88-393.06) | 418.46(266.91-518.94) | <0.001\*\*\*,‡ |
| **IL-6, pg/ml** | 23.01(7.28-94.66) | 39.74(10.50-212.45) | 2479(2332-5781) | 0.001‡‡‡,†† |
| **IL-17A, pg/ml** | 67.43(47.92-105.46) | 20.32(10.05-30.91) | 15.63(12.31-25.82) | <0.001\*\*\*,‡‡ |
| **IL-22, pg/ml** | 71.27(50.21-107.79) | 26.71(12.66-41.68) | 40.6(13.88-42.40) | <0.001\*\*\*,‡ |
| **IL-23, pg/ml** | 551.73(483.23-971.33) | 204.21(132.19-355.40) | 373.25(270.96-677.50) | <0.001\*\*\* |

**Note:** The \* depicts comparison of cluster 1 with cluster 2, ‡ depicts comparison of cluster 1 with cluster 3 and the † depicts comparison of cluster 2 with cluster 3. \*\* *p* < 0.01; \*\*\* *p* < 0.001; ‡ *p* < 0.05; ‡‡ *p* < 0.01; ‡‡‡ *p* < 0.001; †† *p* < 0.01.

**Abbreviations:** TNF, tumor necrosis factor; IL, interleukin.

**Table S3** Clinical characteristics and levels of cytokines at admission of patients with and without smoking history

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Patients with**  **smoking history**  **(n = 70)** | **Patients without**  **smoking history**  **(n = 17)** | ***p*-value** |
| Age, yrs | 72.17 ± 8.149 | 71.24 ± 10.256 | 0.688 |
| Male | 70 (100%) | 12 (70.6%) | <0.001 |
| BMI, kg / m2 | 21.744 ± 2.954 | 20.249 ± 2.892 | 0.070 |
| Comorbidities |  |  |  |
| Diabetes mellitus | 11 (15.7%) | 1 (5.9%) | 0.292 |
| Hyperlipidemia | 3 (4.3%) | 0 (0.0%) | 1.000 |
| Coronary heart disease | 22 (31.4%) | 2 (11.8%) | 0.104 |
| Chronic kidney disease | 2 (2.9%) | 0 (0.0%) | 1.000 |
| Acute exacerbation frequency in  previous 12 months | 3 (1-6) | 2 (1-3.5) | 0.103 |
| Cytokine levels |  |  |  |
| TNF-α, pg/ml | 42.79 (23.13-147.90) | 32.94 (16.28-206.41) | 0.830 |
| IL-4, pg/ml | 59.78 (28.27-104.60) | 63.02 (31.82-110.02) | 0.756 |
| IL-5, pg/ml | 9.50 (3.10-20.07) | 10.33 (1.93-27.00) | 0.777 |
| IL-17E, pg/ml | 390.23 (201.04-715.12) | 461.15 (253.11-663.90) | 0.220 |
| IL-6, pg/ml | 44.63 (10.17-227.94) | 35.41 (8.79-83.47) | 0.567 |
| IL-17A, pg/ml | 25.71 (11.96-48.08) | 33.68 (18.55-46.68) | 0.214 |
| IL-22, pg/ml | 36.18 (19.32-56.70) | 40.60 (20.85-52.72) | 0.589 |
| IL-23, pg/ml | 291.45 (160.09-490.73) | 432.72 (191.96-576.41) | 0.254 |
| Outcome |  |  |  |
| Type I respiratory failure | 13 (18.6%) | 3 (17.6%) | 0.930 |
| Type II respiratory failure | 18 (25.7%) | 5 (29.4%) | 0.756 |
| Non-invasive ventilation | 13 (18.6%) | 2 (11.8%) | 0.505 |
| Tracheal intubation | 1 (1.4%) | 1 (5.9%) | 0.354 |
| In-hospital mortality | 2 (2.9%) | 0 (0.0%) | 1.000 |
| Length of hospital stay, days | 12.5 (10.8-15.0) | 14.0 (9.0-20.0) | 0.826 |

**Abbreviations:** TNF, tumor necrosis factor; IL, interleukin.