RELATIONSHIP BETWEEN RESIDUAL VIREMIA, HIV-DNA, SOLUBLE CD14 AND INFLAMMATORY MARKERS IN HIV-1 POSITIVE PATIENTS RECEIVING ANTIRETROVIRAL THERAPY

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Background: Antiretroviral therapy suppress viral load but HIV infected patients (pts) may have persistent residual viremia (RV) and low grade of inflammation/ immune activation that have been associated with non- AIDS defining events. The impact of persistent RV as well as of HIV DNA load on immune activation/inflammation remain unclear. The purpose of this study was to gain new insights into the relationship between RV, markers of inflammation and HIV DNA levels.

Material/methods: 321 HIV-1 infected pts were retrospectively analyzed for 48 months. Pts were grouped according to viral load (VL) measured during follow up: I pts with undetectable viremia (n=113); II pts who showed viremia detectable but below the threshold value (n=113); III pts with at least 2 values of VL over the threshold value but below 200 copies/ml (n=95). HIVRNA load was quantified by kPCR molecular system. TNF-α, IL-6 and sCD14 were evaluated by ELISA assay. Total HIVDNA was quantify by commercial assay (Biocentric). Differences were evaluated by Mann Whitney test with Bonferroni correction.

Results: There was no significant difference in the proportion of patients with TNF-α quantifiable between groups (TNF-α >8.4 pg/ml: 12,4% in group I; 12,4 % in group II and 7,1 % in group III; p=0,196); in contrast, median plasma concentration of TNF-α was significantly higher in II and III groups than in I [I 7.20 pg/ml (IQR 5.80-9.20) vs II 25 pg/ml (IQR 19-26.30) p=0.046; I vs III 25.6 (IQR 23-30,05) p=0.02] (Figure1A)
The proportion of patients with IL-6 levels higher than the low limit of detection was higher in I than in III (44,2 % vs 24,8%; p<0.0001); no difference about IL-6 levels, among groups were observed. (Figure1B)
Significant differences of sCD14 levels were detected between groups. Specifically, lower levels of sCD14 were detected in I compared to levels in II [7.20 µg/ml (IQR 6-8.95) vs 8.7 µg/ml (IQR 6.8-11) p<0.0001] and in III [10 µg/ml (IQR 9-12.5) p<0.0001]; significant difference between sCD14 levels in II and III (p=0.001) was detected (Figure1C). By multivariate analysis, sCD14 levels were independently associated with age. HIV DNA levels in patients with detectable viremia were significantly higher than those detected in individuals with undetectable viremia [III: 3.05 log copies HIV DNA/10^6 PBMC (IQR 3-3.36) vs I: 2.59 log copies HIV DNA/10^6 PBMC (IQR 2.25-2.88), p<0.0001; II: 2.87 log copies HIV DNA/10^6 PBMC (IQR 2.53-3.18) vs I, p=0.001] (Figure1D). The association between HIV-DNA and residual viremia was confirmed by multivariate analysis.

Conclusions: These data demonstrated that maintaining undetectable viral load in HIV infected patients may reduce inflammation and microbial traslocation markers. However therapy specifically targeting the immune pathway that are activated should be considered to further reduce inflammation and the risk of non-AIDS linked morbidities.

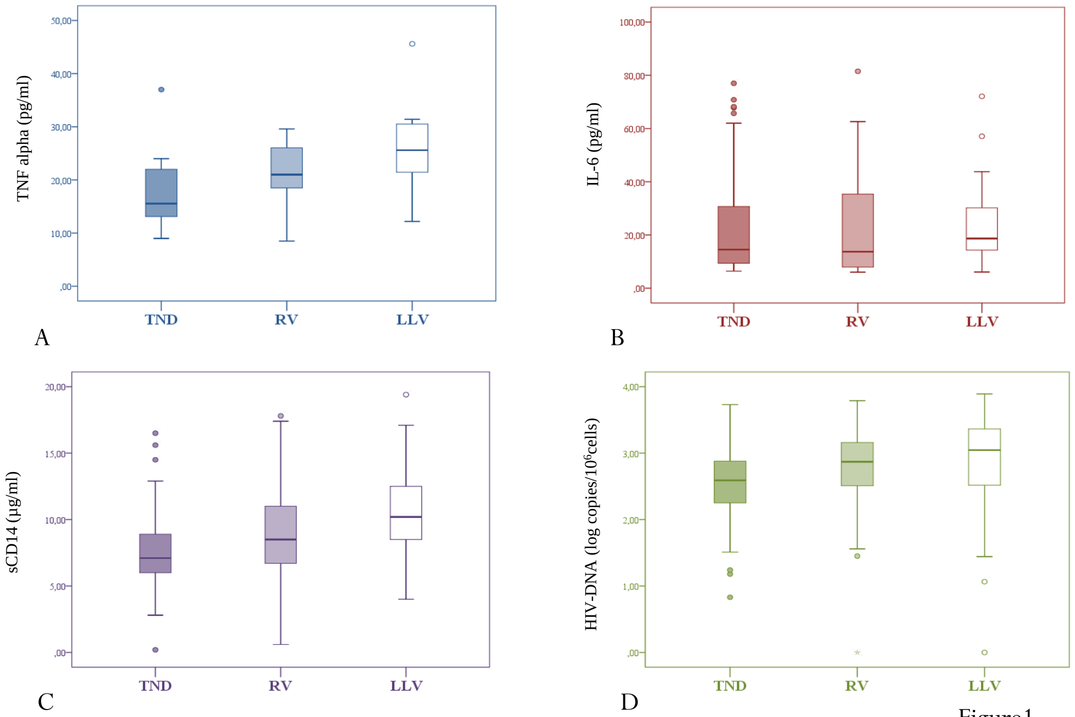

Figure1