

# Mitochondrial Toxicity in Adipose Tissue from HIV-Infected Women during Pregnancy

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**ABSTRACT:** Aim of this study was to analyze mitochondrial (mt) toxicity in HIV+ women due to antiretrovirals taken during pregnancy. mtDNA was quantified in adipose tissue collected during delivery. No correlation was found between mtDNA content and viro-immunological, glucose and lipidic parameters, nor with the type of drugs assumed during pregnancy, indicating that treatment were not toxic.

**BACKGROUND:** Increasing number of pregnant HIV+ women are receiving combination of antiretroviral regimens for prevention of mother-to-child virus transmission or for treatment of the infection itself. Several studies have demonstrated that NRTI induce mitochondrial (mt) toxicity by several mechanisms, including depletion of mtDNA, whose levels are considered a marker of NRTI toxicity. By the quantification of mtDNA levels, we studied the role of mt toxicity in HIV+ women during pregnancy and the possible correlation with antiretroviral regimen, viro-immunological and metabolic parameters.

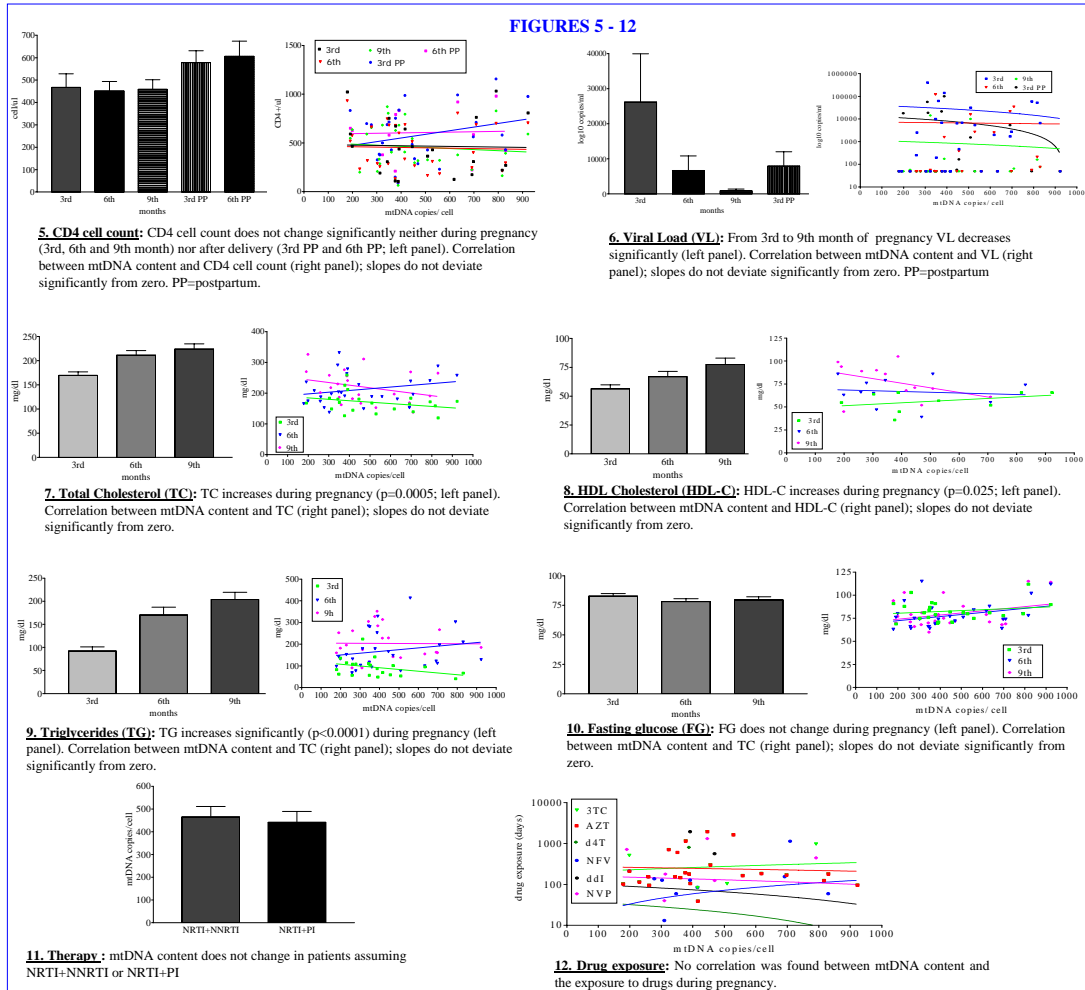
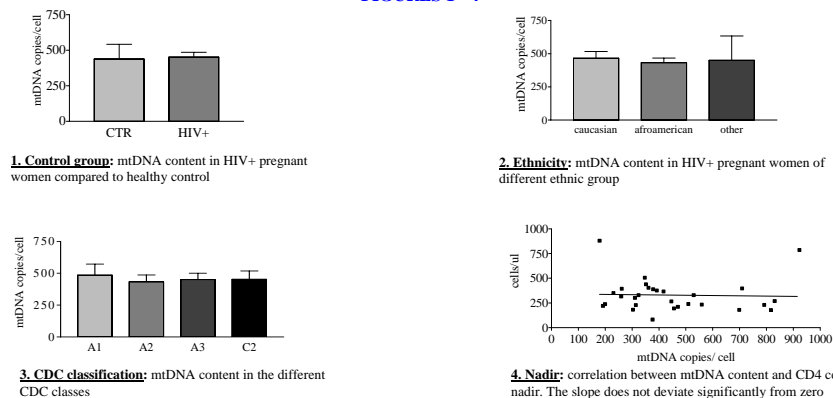
**SUBJECTS:** HIV+ women were enrolled in the framework of the Italian Prospective Cohort Trial on Efficacy and Toxicity of Antiretroviral in Pregnancy (TARGET study). We analyzed 36 patients (mean age 32.6 years; 55.5% caucasian, 36.1% afroamerican, 2.8% hispanic and 5.6% other), that were in CDC (Classification System for HIV Infection of Centers for Disease Control and Prevention) class A1 (25.0%), A2 (41.7%), A3 (25.0%) and C2 (8.3%). During pregnancy, 25 patients were treated with Lamivudine (3TC), 21 with Zidovudine (AZT), 9 with Combivir (AZT+3TC) and 4 with Abacavir (ABC); 2 received Didanosine (ddI), 2 Stavudine (d4T) and only 2 both ddI and d4T; 16 assumed Nevirapine (NVP), 8 Nelfinavir (NFV), 4 Lopinavir/ritonavir (LT) and 4 Tenofovir (TDF). At 3rd, 6th and 9th month of pregnancy we collected data on: CD4 count, plasma HIV RNA, total and HDL-cholesterol, fasting glucose and triglycerides. Data were collected also on 3rd and 6th months after delivery (postpartum; PP).

**METHODS:** By using a Real Time PCR approach (mtDNA qPCR kit from GeneMoRe Italy SRL, Modena, Italy), we quantified mtDNA copies per cell in subcutaneous fat samples collected during delivery. As control we studied fat sample from aesthetic plastic surgery of 10 age-matched healthy women. Statistical analysis was performed by Kruskal-Wallis test and correlation was evaluated using Linear Regression test (Prism 3.03). A p value <0.05 was considered significant.

**RESULTS:** The mean mtDNA copies per cell were 452±198 (mean±SD, range 178-922). Such value is similar to that found in subcutaneous fat from 10 age- and sex-matched healthy subjects (378±229; figure 1). mtDNA content does not change among different ethnic groups or CDC classes (figures 2 and 3). During pregnancy, CD4 cell count does not change (figure 5, left panel) while HIV RNA decrease significantly (figure 6, left panel). Moreover, total- and HDL-cholesterol and triglycerides increase significantly (figures 7-9, left panel), while fasting glucose remained constant (figure 10, left panel).

We found no association between mtDNA and CD4 cell count Nadir (figure 4), CD4 cell count during pregnancy (figure 5, right panel), HIV RNA (figure 6, right panel), total and HDL-cholesterol (figures 7 and 8, right panel), fasting glucose and triglycerides (figures 9 and 10, right panel) and use of PI or NNRTI in association with NRTI (figure 11). No correlation was found between mtDNA and exposure to drugs during pregnancy (figure 12).

FIGURES 1 - 4



**CONCLUSION:** No association was found between mtDNA and CD4 cell count, HIV RNA or CD4 cell count nadir. No association was observed with mtDNA levels and glucose or lipidic parameters. No correlation was found between mtDNA and exposure to drugs. The therapy did not cause changes in adipose tissue mtDNA content, suggesting that treatment is apparently devoid of relevant mitochondrial toxicity.