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# HETEROGENEITY OF IRON STATUS AND ANTIRETROVIRAL THERAPY DURING PREGNANCY IN CÔTE D'IVOIRE

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**ABSTRACT**: Antiretroviral therapy for decades is the appropriate treatment for infected populations with human immunodeficiency virus (HIV). However, it is associated with complications that affect the organism infected. The combination of antiretroviral therapy and pregnancy degrades iron metabolism. This work aims to evaluate and characterize the impact of the interaction between antiretroviral therapy and different stages of pregnancy in women of Abidjan on all biological indicators of iron status. The conducted investigations were a prospective, cross-sectional, descriptive analytical and case-control study. They concerned 275 women of reproductive age in all trimesters of pregnancy and in consultation to integrated center for bioclinical research of Abidjan (ICBRA). These women were divided into two groups: 135 pregnant women infected with HIV without antiretroviral therapy as controls and 140 pregnant women infected with HIV receiving antiretroviral therapy. All biological indicators of iron metabolism were determined either by colorimetric or immunoturbidimetric assays through blood samples from each pregnant woman or by calculation. The Student t test, factor analysis of variance (ANOVA) with two factors and the G test or log likelihood ratio test with Statistica Statsoft Windows version 7.1 and software R.2.0.1 Windows version were used for the statistical analyzes data. The level of significance was defined for a p value $< 0.05$. The results of the study showed an extreme degradation in all evaluation of iron metabolism biological indicators assessment in all pregnant women. Analyzes of these biological parameters revealed that pregnant women with HIV and receiving treatment showed a significant alteration of their iron status (92 %) against 62.9 % in control pregnant women. However, latter have indicated a strong immunodepression towards the end of pregnancy with 40 % against 28 % among women on antiretroviral therapy. In addition, control subjects in early pregnancy reported a high rate of inflammatory anaemia associated with iron deficiency (30 % against 0 %) to critical stage (stage C) of HIV infection progression. The interaction between antiretroviral therapy and pregnancy disrupted iron metabolism in pregnant women infected with HIV. This deterioration is greater in infected pregnant women without antiretroviral therapy. The probable reasons for these changes in iron status of pregnant women infected with HIV in Abidjan are pregnancy and antiretroviral medication.

**INTRODUCTION:** Antiretroviral therapy is considered to be appropriate and adapted treatment to population infected with human immuno-deficiency virus (HIV). It is based on an arsenal of drugs to multiple properties reducing and neutralizing activity of HIV on the infected organism [1]. In addition, this treatment in infected has shown its effectiveness in the world [2].

Thus, antiretroviral therapy has emerged as a way to reduce the infection rate among the population and even acting as a preventive medicine in individuals who may have been exposed to the virus [3]. However, its administration to the infected population is associated with complex complications. Several studies worldwide have shown in all compartments of the body diseases with antiretroviral therapy [4, 5]. These are disturbances of lipid, protein, glucides profiles and even heart disease [6].

Worse, this alteration of physiological functions associates the degradation of essential micronutrients metabolism in the body such as iron [7, 8, 9]. They cover all classes and strata of the population especially women of reproductive age. The most vulnerable among women of reproductive age are pregnant women [10, 11, 12]. Women infected with HIV during pregnancy are a high-risk population. Despite antiretroviral therapy and taking antianaemic, iron metabolism is greatly affected during pregnancy [13, 14].

Numerous works in developing countries especially in Africa have reported that antiretroviral therapy would cause anaemia during pregnancy. The impact of anaemia on pregnancy is disastrous for the mother and the fetus. It leads to serious consequences such as the physical integrity of the mother, retarded growth of the fetus in the womb, underweight of newborn at birth and preterm delivery [15, 16, 17, 18].

In Côte d'Ivoire, few studies have indicated the influence of antiretroviral therapy in women during pregnancy [19]. Similarly there is no information available on the impact of the interaction between antiretroviral therapy and pregnancy across biological indicators of iron metabolism.

In vision of the global strategy of the health sector on HIV/AIDS 2011-2015, envisaged by the United Nations on AIDS, all aspects unexplored and not prospected should be subject to studies [20, 21].

This is the case of antiretroviral therapy and heterogeneity of iron status during pregnancy in Côte d'Ivoire.

This study aims to identify and characterize a possible influence of antiretroviral therapy on biological indicators of iron metabolism assessment and eventual interaction of antiretroviral therapy and pregnancy on these biological parameters. This work has specific objectives to:

- Compare depending on the trimester.different biological parameters of iron status between the two groups of women;
- Identify and compare the different proportions of main biological parameters according to the women's group and the three trimesters of pregnancy;
- Report and compare the different prevalences of iron metabolism components by trimesters of pregnancy between the two groups of women;
- Reveal the group of infected pregnant women which was most exposed to a possible alteration of iron metabolism;
- Observe the components' evolution of iron status during HIV infection progression in women during pregnancy;
- Indicate the stage of pregnancy during which the interaction of antiretroviral therapy and pregnancy greatly influences the iron status of women.

## MATERIALS AND METHODS:

**Study population:** The investigations were cross-sectional and descriptive study which took place from 21 October 2009 to 21 December 2012 in the Integrated Centre for Bioclinical Research of Abidjan (ICBRA). The study involved 275 women aged from 18 to 45 years with mean age of 28.1 ± 0.7 years during pregnancy. This sample of pregnant women consists of 135 control subjects without antiretroviral treatment and 140 HIV-infected women receiving antiretroviral therapy. These pregnant women came for consultation in Integrated Centre for Bioclinical Research of Abidjan (ICBRA) for prenatal examinations and biological monitoring of their HIV infection for some.

Control pregnant women were composed of 50 subjects in the first trimester, 45 in the second trimester and 40 subjects in the last trimester (**Figure 1**). Women infected with HIV and on antiretroviral therapy from at least one year are composed of 40 subjects in the first trimester, 45 subjects in the second trimester and 55 women in the last trimester. In addition, this group of women included 99 % of HIV-1 against 1 % HIV-2. Tritherapy most widely prescribed to pregnant women is characterized by Zidovudine (AZT), Lamivudine (3TC) and Nevirapine (NVP). This set of women from different municipalities and suburbs of Abidjan (Côte d'Ivoire) was selected after informed consent of each woman on the objectives of the investigation. The 275 selected pregnant women have not presented major complications of hypertension, diabetes, rheumatoid arthritis. In contrast, those with recently reported major health concerns that is transfused, indicating digestive and gynecological diseases were excluded.

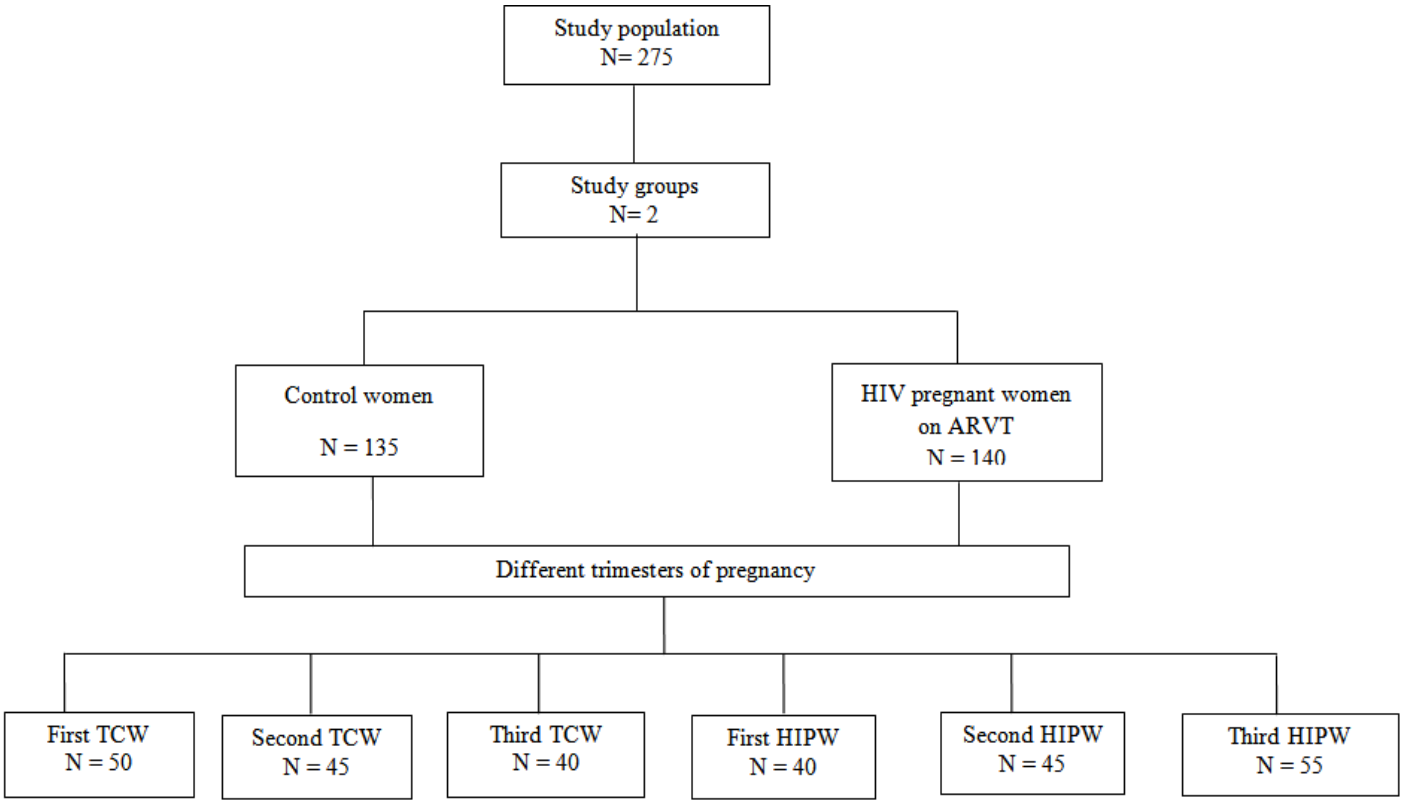


**FIGURE 1: SAMPLING OF STUDY POPULATION ACCORDING TO SELECTED SITES AND DIFFERENT TRIMESTERS OF PREGNANCY.** N: Total number of each subject group; TCW: Trimester control women; HIPW: HIV pregnant women

The mean age of enrolled women in the study was 25.3 ± 0.5 years and 30.8 ± 0.9 years respectively in control subjects and HIV infected women with antiretroviral treatment. Control subjects included more adolescents (28.5 %) compared to women receiving antiretroviral therapy (2 %). These had generally a body mass index (BMI) of 24.6±0.6 $kg.m^{-2}$ 54% of women had normal weight status against 46% for abnormal weight status with underweight (14%) and 32% overweight. In controls, mean BMI was 23.9±0.4 $kg.m^{-2}$ 52.6% indicated a normal weight status against 47.4 % for abnormal weight status with underweight (17.8%) and 29.6 % overweight (**Table 1**).

The gravidity and parity had mean values of 1.8 ± 0.2 and 1.8±0.2 in women with ART and 3 ± 0.1 and 1.4±0.1 for control subjects. Several study subjects (106 and 84 respectively) had indicated a pregnancy for their obstetric histories. In this same way, respectively 62.2% and 94% of women selected had at least one childbirth.

In terms of space between births, 67.4 % of control women against 56 % of infected women have observed less than 3 years between pregnancies. Study population also included married, Widows, single and subjects living in concubinage (Table 1).

**TABLE 1: GENERAL CHARACTERISTICS OF THE STUDY POPULATION**

| Anthropometric and sociodemographic parameters | Control women N = 135 | HIV pregnant women/ARVT N = 140 |
|---|---|---|
| | n (%) | n (%) |
| **Age (years)** | 25.3 ± 0.5 | 30.8 ±0.9 |
| 18 – 19 | 25 (28.5) | 3 (2) |
| 20 – 45 | 110 (81.5) | 137 (98) |
| **BMC (kg.m$^{-2}$)** | 23.9 ± 0.4 | 24.6 ± 0.6 |
| < 19.8 | 24 (17.8) | 20 (14) |
| 19.8 – 26 | 71 (52.6) | 76 (54) |
| > 26 | 40 (29.6) | 44 (32) |
| **Gravidity** | 3 ± 0.1 | 1.8 ± 0.2 |
| **Primigravidae** | 29 (21.5) | 56 (40) |
| **Multigravidae** | 106 (78.5) | 84 (60) |
| **Parity** | 1.4 ± 0.1 | 1.8 ± 0.2 |
| **Nulliparous** | 51 (37.8) | 8 (6) |
| **Primiparous** | 33 (24.4) | 56 (40) |
| **Multiparous** | 51 (37.8) | 76 (54) |
| **Space between births (Months)** | 26.7 ± 2.6 | 30.8 ± 8.9 |
| < 36 | 91 (67.4) | 78 (56) |
| > 36 | 44 (32.6) | 62 (44) |
| **Matrimonial status** | | |
| Married | 13 (9.6) | 39 (28) |
| Widowed | 13 (9.6) | 8 (6) |
| Single | 48 (35.6) | 37 (26) |
| Concubinage | 61 (45.2) | 56 (40) |
| **Education attainment** | | |
| Uneducated | 47 (34.8) | 25 (18) |
| Primary school | 36 (26.7) | 31 (22) |
| Secondary school | 52 (38.5) | 42 (30) |
| Superior | 0 (0) | 42 (30) |

N: Total number of each subject group; n: Number of observed subject in each group

**Blood samples and assays of Biological parameters:** For each of the recruited women, a blood sample was collected in dry tubes and tubes with 5 ml anticoagulant each were performed fasting bend of the elbow in the morning. Whole blood collected in tubes with anticoagulant (EDTA) achieved the CD4 counts by flow cytometry with Fascalibur® and the blood count by the Sysmex PLC Xt 2000i. The collected blood in dry tubes was centrifuged at 3000 tours for 5 minutes to obtain the serum. The obtained serum allowed determining HIV status and biochemical data assessment of iron status. For HIV serology, the method most used in the care centers is the use of two successive tests.

Once the first test (Determine) is positive, we proceed to discrimination test (Genie II HIV-1/HIV-2) to determine the type of HIV. The quantitative determination of biochemical parameters (serum iron. serum transferrin and serum ferritin) in human serum is based on a colorimetric technique available on most automated COBAS INTEGRA 400. For this determination, the COBAS INTEGRA kits Iron (IRON). Tina-quant Transferrin ver.2 (TRSF2) TRSF2 test and Ferritin Gen.2 ID 0-567 test (FERR2). ID 0-567 test containing *in vitro* diagnostic reagents were used. The total iron binding capacity (TIBC) and the saturation coefficient of transferrin (SCT) were obtained by calculations.

**Evaluation and Statistical analysis of Biological parameters:** To better appreciate the parameters of biological assays, conventional criteria were selected. They associated the recommendations of international organizations (WHO). French Society of Clinical Biology (SFBC/France), French Society of Hematology (SFH/France-Group of Cellular Haematology), Society of Nutrition and Diet of the French Language (France), Centre for Disease Control and Prevention (WHO/CDCP) and Institute of Medicine [22, 23, 24, 25].

The Student t test for independent samples was used to estimate possible changes of biological indicators of iron status in two groups of HIV infected pregnant women. The obtained values of the biological parameters of iron status were subjected to a factorial analysis of variance (ANOVA) with two factors (the three trimesters of pregnancy and antiretroviral therapy) in order to evaluate one hand, their evolution during different trimesters in infected control pregnant women.

And secondly, these tests aimed to reveal an eventual influence of antiretroviral treatment on biological indicators of iron metabolism in two groups of selected pregnant women. These statistics treatments with Statistica Statsoft program Windows version 7.1 were associated NEWMAN-KEULS as multivariate test post hoc to specify the probable groups of women significantly different [26]. Different observed proportions of biological indicators of iron status were compared by the G test or log Likelihood ratio test with the software R.2.0.1 Windows version [27]. The level of significance was defined for a p value < 0.05.

**Ethics:** Experimental procedures and protocols used in this study were approved by ethical committee of Health Sciences (Nangui Abrogoua University). These guide lines were in accordance with the internationally accepted principles for laboratory use and care. Approval was also obtained from the Ministry of Higher Education and Scientific Research and the Ministry of Health and Public Hygiene in the Republic of Côte d'Ivoire.

## RESULTS:

**Evolution of iron status biological parameters:** The study results in **Table 2** showed that all blood counts parameters were abnormal compared with reference values in both groups of women. In the same way, MCV in control women (77.1±0.8 fl) and MCHC in infected pregnant women receiving ART (31.4±0.2 g/dl) were also abnormal compared to standards. Conversely, other erythrocyte indices indicated normal values compared with references in all infected pregnant women.

For biochemical indicators and CD4, all determined values were normal according to standards except saturation coefficient of transferrin (9.5±0.5 % and 10.9 ± 0.7 % respectively).

**TABLE 2: MEAN VALUES OF IRON STATUS BIOLOGICAL PARAMETERS IN THE TWO INFECTED WOMEN GROUP**

| Biological parameters of iron status | Control women N = 135 | HIV Pregnant women ARVT N = 140 | p-values | Reference values[α] |
|---|---|---|---|---|
| **Red blood cell counts** | | | | |
| Red blood cells ($10^{12}$/l) | 3.8 ± 0.1 | 3.7 ± 0.1 | 0.3 (NS) | 4-5.4 |
| Hemoglobin (g/dl) | 10 ± 0.2 | 10 ± 0.2 | 1 (NS) | 10.5-14 |
| Hematocrit (%) | 29.3 ± 0.6 | 31.9 ± 0.6 | 0.2 (NS) | 32-45 |
| **Erythrocyte indices** | | | | |
| MCV (fl) | 77.1 ± 0.7 | 87 ± 1.7 | 0.04 **(S)** | 80-100 |
| MCH (pg) | 26.1 ± 0.3 | 27.5 ± 0.6 | 0.3 (NS) | 27-31 |
| MCHC (g/dl) | 33.3 ± 0.2 | 31.4 ± 0.2 | 0.4 (NS) | 32-36 |
| **Plasma compartment** | | | | |
| Serum iron (µmol/l) | 9.5 ± 0.3 | 13.1 ± 0.7 | 0.04 **(S)** | 6.6-26 |
| Serum transferrin (g/l) | 4.3 ± 0.2 | 3 ± 0.1 | 0.2 (NS) | 2-3.6 |
| Total iron binding capacity (µmol/l) | 107.8 ± 5.9 | 74.8 ± 3.5 | 0.03 **(S)** | 50-90 |
| Saturation coefficient (%) | 9.5 ± 0.6 | 10.9 ± 0.7 | 0.2 (NS) | 15-35 |
| **Iron stores compartment** | | | | |
| Serum ferritin (µg/l) | 52.8 ± 2 | 99.4 ± 15.3 | 0.01 **(S)** | 15-150 |
| **Immunological parameter** | | | | |
| CD4 (cellules/µl) | 449 ± 17.9 | 347.1 ± 27.5 | 0.001 **(S)** | 200-500 |

MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular concentration of hemoglobin concentration; ARVT: Antiretroviral therapy; α: Reference values of the assessment biological parameters of iron status in women during pregnancy (Vernet *et al*.. 2001; IOM/US. 1990; UNICEF/UNU/WHO. 2001; SNDLF. 2001; WHO/CDCP. 2004); S: Difference statistically significant for p < 0.05; NS: Difference not statistically significant for p < 0.05.

Analyses of comparison between the two groups of women generally showed statistically significant differences in MCV (p = 0.04), serum iron (p = 0.04), TIBC (p = 0. 03), serum ferritin (p = 0.01) and CD4 (p = 0.001). However, other biological parameters of iron status reported no significant difference (p > 0.05) between the two groups of infected pregnant women. Thus, MCV, serum iron and serum ferritin in infected pregnant women on antiretroviral therapy were more increased than in control women.

In contrast, CD4 and TIBC have been significantly lower in these pregnant women receiving antiretroviral treatment than the control women.

The significant evolution of blood count cells parameters (red blood cells, hemoglobin and hematocrit). MCV, MCH, serum iron and saturation coefficient of transferrin in the controls during pregnancy was decreased (**Table 3**). In contrast, serum transferrin, TIBC, iron stores and CD4 were significantly (p < 0.05) increased during pregnancy in these women compared with infected pregnant women on antiretroviral therapy.

Multiple statistical treatments showed a significant (p < 0.05) interaction between antiretroviral therapy and pregnancy in three haematological parameters (hemoglobin. hematocrit and MCV) and all biochemical indicators of iron metabolism except serum transferrin. Thus, hemoglobin was low in the first trimester of pregnancy in infected women on antiretroviral therapy (ARVT) compared with control women. However, at the beginning and at the end of pregnancy, infected pregnant women reported hematocrit values significantly (p < 0.05) higher compared to control women. In the same vein, VGM in pregnant women on ARVT was strongly greatest throughout the three trimesters compared with control women.

**TABLE 3: CHANGES OF BIOLOGICAL PARAMETERS ACCORDING TO DIFFERENT INFECTED WOMEN GROUPS DURING PREGNANCY**

| Biological parameters | Different trimesters of pregnancy | | | | | |
|---|---|---|---|---|---|---|
| | First | | Second | | Third | |
| | Control women N = 50 n (%) | HIV Pregnant women ARVT N = 40 n (%) | Control women N = 45 n (%) | HIV Pregnant women ARVT N = 45 n (%) | Control women N = 40 n (%) | HIV Pregnant women ARVT N = 55 n (%) |
| **Red blood cell counts** | | | | | | |
| Red blood cells ($10^{12}$/l) | 4 ± 0.1a | 3.8 ± 0.2 | 3.8 ± 0.1a | 3.8 ± 0.1 | 3.5 ± 0.1b | 3.6 ± 0.1 |
| Hemoglobin (g/dl) | 10.8 ± 0.2a | 10.3 ± 0.5* | 9.9 ± 0.3b | 10.2 ± 0.4 | 9.1 ± 0.3c | 10 ± 0.2 |
| Hematocrit (%) | 31.7 ± 0.7a | 33.3 ± 1.7* | 29.9 ± 1a | 32.2 ± 1.1 | 25.7 ± 1.1b | 31.7 ± 0.7* |
| **Erythrocyte indices** | | | | | | |
| MCV (fl) | 79.3 ± 1.2a | 87.6 ± 1.4* | 78.3 ± 1.2a | 85.2±3.1* | 72.9 ± 1.1b | 89.1 ± 2.4* |
| MCH (pg) | 27.3 ± 0.4a | 27.2 ± 0.4 | 26.1 ± 0.5a | 26.9±1.3 | 24.6 ± 0.4b | 28.5 ± 0.8 |
| MCHC (g/dl) | 33.8 ± 0.3 | 31 ± 0.4* | 33.5 ± 0.2 | 31.5± 0.5* | 32.4 ± 0.5 | 31.7 ± 0.2 |
| **Plasma compartment** | | | | | | |
| Serum iron (µmol/l) | 12.7 ± 0.5a | 11.1 ± 1.4 | 8.7 ± 0.4b | 11.8±1.4 | 6.3 ± 0.3c | 14.5 ± 1.3** |
| Serum transferrin (g/l) | 3.2 ± 0.1b | 2.3 ± 0.1 | 4.2 ± 0.4b | 3 ± 0.3 | 5.8 ± 0.6a | 3.1 ± 0.2 |
| Total iron binding capacity (µmol/l) | 80.4 ± 3.5c | 57.9 ± 3* | 104.5 ± 10.1b | 74.6 ± 6.6 ** | 145.9 ± 14.1a | 78.2 ± 4.6** |
| Saturation coefficient (%) | 14.9 ± 1.1a | 10.4 ± 1 | 7.6 ± 0.9b | 9.8 ± 1.2 | 4.8 ± 0.5c | 11.8 ± 1.2** |
| **Iron stores compartment** | | | | | | |
| Serum ferritin (µg/l) | 75.1 ± 2.5a | 122.1±47.8*** | 49.3 ± 1.9b | 92.8 ± 29.4*** | 29 ± 0.8c | 90.8±17.4*** |
| Immunological parameter | | | | | | |
| CD4 (cellules/µl) | 675.7 ± 14.5a | 296.6 ± 13.2*** | 409.8 ± 7.9c | 395.9 ± 11.4b | 209.7 ± 12.3c | 338 ± 8.3 * |

N: Total number of each women group; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular concentration of hemoglobin concentration; ARVT: Antiretroviral therapy; *: Difference statistically significant for p < 0.05; a. b. c and d: Women groups statistically different for p < 0.05; **: Difference statistically significant for p < 0.01; ***: Difference statistically significant for p < 0.001

For biochemical parameters and CD4 a significant interaction ($p < 0.05$) between antiretroviral therapy and pregnancy has been observed in study population at the last trimester of pregnancy except for serum transferrin. Thus, infected women on ART reported values significantly ($p < 0.01$) greater iron and saturation that women witnesses except at the total capacity of fixation (Table 3). Another interaction between antiretroviral therapy and all trimesters of pregnancy was reported in regard to the total capacity of attachment and serum ferritin throughout pregnancy. Therefore, iron stores of pregnant women on ART were significantly ($p <0.001$) was higher compared to control women in all trimesters of pregnancy (Table 3).

**Distributions of proportions of iron status main parameters:** In **table 4**, the two groups of pregnant women infected with HIV have indicated significant differences ($p < 0.05$) for microcytosis, macrocytosis, proportions of women with low values of transferrin (< 2 g / l) and ferritin (< 15 l / dl). In the same way, the controls have recorded the prevalences of microcytosis, high values of transferrin, of TIBC and of CD4 greater than infected pregnant women on ARVT. However, women on ARVT have more indicated macrocytosis (24.3 %), proportion of low values of ferritin (8.6 %) and CD4 (28.6 %) compared with control women.

**TABLE 4: MAIN BIOLOGICAL PARAMETERS PROPORTIONS OF THE TWO INFECTED WOMEN GROUP**

| Biological parameters | Control women N = 135 n (%) | HIV Pregnant women ARVT N = 140 n (%) | p-values |
|---|---|---|---|
| **Hemoglobin (g/dl)** | | | |
| < 11 ou < 10.5 | 84 (62.2) | 100 (71.4) | 0.4 (NS) |
| > 11 ou > 10.5 | 51 (37.8) | 40 (28.6) | 0.2 (NS) |
| **Hematocrit (%)** | | | |
| < 33 ou < 32 | 88 (65.2) | 73 (52.1) | 0.2 (NS) |
| > 33 ou > 32 | 47 (34.8) | 67 (47.9) | 0.1 (NS) |
| **MCV (fl)** | | | |
| < 80 | 88 (65.2) | 34 (24.3) | $1.1.10^{-5}$ (S) |
| 80-100 | 47 (34.8) | 72 (51.4) | 0.07 (NS) |
| > 100 | 0 (0) | 34 (24.3) | $6.5.10^{-9}$ (S) |
| **MCH (pg)** | | | |
| < 27 ou > 31 | 90 (66.7) | 89 (63.6) | 0.8 (NS) |
| < 27 ou > 31 | 45 (33.3) | 51 (36.4) | 0.7 (NS) |
| **Serum iron (µmol/l)** | | | |
| < 6.6 | 24 (17.8) | 15 (10.7) | 0.2 (NS) |
| 6.6-26 | 111 (82.2) | 123 (87.9) | 0.7 (NS) |
| > 26 | 0 (0) | 2 (1.4) | 0.2 (NS) |
| **Serum transferrin (g/l)** | | | |
| < 2 | 6 (4.5) | 9 (6.4) | 0.6 (NS) |
| 2-3.6 | 89 (65.9) | 125 (89.3) | 0.06 (NS) |
| > 3.6 | 40 (29.6) | 6 (4.3) | $4.1.10^{-6}$ (S) |
| **TIBC (µmol/l)** | | | |
| < 50 | 6 (4.5) | 9 (6.4) | 0.6 (NS) |
| 50-90 | 89 (65.9) | 112 (80) | 0.2 (NS) |
| > 90 | 40 (29.6) | 19 (13.6) | 0.01 (S) |
| **SCT (%)** | | | |
| < 15 | 105 (77.8) | 119 (85) | 0.6 (NS) |
| 15-35 | 30 (22.2) | 19 (13.6) | 0.1 (NS) |
| > 35 | 0 (0) | 2 (1.4) | 0.2 (NS) |
| Serum ferritin (µg/l) | | | |
| < 15 | 0 (0) | 12 (8.6) | 0.0006 (S) |
| 15-150 | 135 (100) | 103 (73.6) | 0.04 (S) |
| > 150 | 0 (0) | 25 (17.9) | $6.3.10^{-7}$(S) |
| **CD4 (cellules/µl)** | | | |
| < 200 | 16 (11.9) | 40 (28.6) | 0.008 (S) |
| 200-499 | 67 (49.6) | 74 (52.9) | 0.7 (NS) |
| ≥ 500 | 52 (38.5) | 26 (18.6) | 0.008 (S) |

MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular concentration of hemoglobin concentration; ARVT: Antiretroviral therapy; TIBC: Total iron binding capacity; SCT: Saturation coefficient of transferrin; S: Difference statistically significant for $p < 0.05$; NS: Difference not statistically significant for $p < 0.05$.

In addition, the results have showed that 184 women of study population (66.9 %) were anaemic. But no significant difference was observed between the two groups of infected women of study (Table 4).

Throughout the pregnancy, an interaction between the three trimesters of pregnancy and antiretroviral therapy was significantly observed on proportion of erythrocyte parameters. Thus, high prevalences of anaemia were reported during first and third trimesters of pregnancy in infected women on ARVT (90 % and 84 % respectively). In contrast, anaemia was lower in second trimester of pregnancy in these women than the controls (40 % against 51.1 % respectively). Moreover, only infected women on ARVT have revealed macrocytosis to last two trimesters of pregnancy (6.7 % and 56 % respectively).

Furthermore, these women have presented higher prevalence of hypochromia during the second trimester of pregnancy than the controls (**Table 5**). The results of study have indicated that, control women were concerned by microcytosis throughout the pregnancy and hypochromia to first and third trimester of pregnancy compared with infected women on ARVT. According changes of erythrocyte parameters, hypochromic microcytic anemia (HMA), normochromic normocytic anaemia (NNA), hypochromic normocytic anaemia (HNA) and normochromic microcytic anaemia (NMA) were observed in study population. Throughout the pregnancy, HMA and HNA then NMA to first trimester of pregnancy were more observed in control women compared with women on ARVT. In contrast, infected pregnant women on ARVT have recorded for the three trimesters, NNA and HNA then NMA for second and third trimesters of pregnancy (Table 5).

**TABLE 5: COMPARED PROPORTIONS OF ERYTHROCYTE PARAMETERS DEPENDING ON DIFFERENT TRIMESTERS OF PREGNANCY**

| Erythrocyte parameters | Different trimesters of pregnancy | | | | | |
|---|---|---|---|---|---|---|
| | First | | Second | | Third | |
| | Control women N = 50 n (%) | HIV Pregnant women ARVT N = 40 n (%) | Control women N = 45 n (%) | HIV Pregnant women ARVT N = 45 n (%) | Control women N = 40 n (%) | HIV Pregnant women ARVT N = 55 n (%) |
| **Red blood cell counts** | | | | | | |
| **Hemoglobin (g/dl)** | | | | | | |
| < 11 ou < 10.5 | 30 (60)b | 36 (90)** | 23 (51.1)b | 18 (40)* | 31 (77.5)a | 46 (84)* |
| > 11 ou > 10.5 | 20 (40)b | 4 (10)*** | 22 (48.9)b | 27 (60)* | 9 (22.5)a | 9 (16)* |
| Hematocrit (%) | | | | | | |
| < 33 ou < 32 | 29 (58)b | 16 (40)** | 28 (62.2)b | 24 (53.3)* | 31 (77.5)a | 33 (60)** |
| > 33 ou > 32 | 21 (42)a | 24 (60)** | 17 (37.8)a | 21 (46.7)* | 9 (22.5)b | 22 (40)*** |
| **Erythrocyte indices** | | | | | | |
| **MCV (fl)** | | | | | | |
| < 80 | 28 (56)b | 8 (20)*** | 28 (62.2)b | 15 (33.3)** | 32 (80)a | 11 (20)*** |
| 80-100 | 22 (44)a | 32 (80)*** | 17 (37.8)a | 27 (60)** | 8 (20)b | 13 (24) |
| > 100 | 0 (0) | 0 (0) | 0 (0) | 3 (6.7)* | 0 (0) | 31 (56)*** |
| **MCH (pg)** | | | | | | |
| < 27 ou > 31 | 26 (52)c | 16 (40)* | 31 (68.9)b | 36 (80)* | 33 (82.5)a | 37 (68)* |
| 27-31 | 24 (48)a | 24 (60)* | 14 (31.1)b | 9 (20)* | 7 (17.5)c | 18 (32)** |
| **Types of anaemia** | | | | | | |
| HMA | 17 (56.7)b | 9 (25)** | 23 (100)a | 10 (60)* | 31 (100)a | 11 (25)*** |
| NNA | 6 (20)a | 27 (75)*** | 0 (0)b | 4 (20)** | 0 (0)b | 10 (20)*** |
| HNA | 4 (13.3)a | 0 (0)** | 0 (0)b | 4 (20)** | 0 (0)b | 25 (55)*** |
| NMA | 3 (10)a | 0(0)* | 0 (0)b | 0 (0) | 0 (0)b | 0 (0) |

N: Total number of each women group; n: Subjects' number observed in each group; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular concentration of hemoglobin concentration; ARVT: Antiretroviral therapy; HMA: Hypochromic Microcytic Anaemia; NNA: Normochromic Normocytic Anaemia; HNA: Hypochromic Normocytic Anaemia; NMA: Normochromic Microcytic Anaemia; *: Difference statistically significant for $p < 0.05$; a, b and c: Women groups statistically different for $p < 0.05$; **: Difference statistically significant for $p < 0.01$; ***: Difference statistically significant for $p < 0.001$.

In **table 6**, the proportions according to reference values limits of biochemical parameters, an interaction of pregnancy and antiretroviral therapy (ARVT) was revealed. Thus, no woman on ARVT has indicated ferritin value below 15µg/l. In the same way, all control women have reported normal ferritin values between 15 and 150µg/l during the three trimesters of pregnancy.

Table 6: Distribution of proportions of biochemical iron status parameters depending on different trimesters of pregnancy

| Biochemical parameters of iron status | Different trimesters of pregnancy | | | | | |
|---|---|---|---|---|---|---|
| | First | | Second | | Third | |
| | Control women N = 50 n (%) | HIV Pregnant women ARVT N = 40 n (%) | Control women N = 45 n (%) | HIV Pregnant women ARVT N = 45 n (%) | Control women N = 40 n (%) | HIV Pregnant women ARVT N = 55 n (%) |
| **Serum iron (µmol/l)** | | | | | | |
| < 6.6 | 4 (8)b | 4 (10) | 5 (11.1)b | 9 (20)* | 15 (37.5)a | 2 (4)*** |
| 6.6-26 | 46 (92)a | 36 (90) | 40 (88.9)a | 36 (80)* | 25 (62.5)b | 51 (92)** |
| > 26 | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (4)* |
| **Serum transferrin (g/l)** | | | | | | |
| < 2 | 0 (0)c | 4 (10)* | 2 (4.4)b | 3 (6.7) | 4 (10)a | 2 (3.6)* |
| 2-3.6 | 39 (78)a | 36 (90)* | 33 (73.3)a | 42 (93.3)* | 17 (42.5)b | 47 (85.5)** |
| > 3.6 | 11 (22)b | 0 (0)** | 10 (22.3)b | 0 (0)*** | 19 (47.5)a | 6 (10.9)*** |
| **TIBC (µmol/l)** | | | | | | |
| < 50 | 0 (0)c | 4 (10)* | 2 (4.4)b | 3 (6.7) | 4 (10)a | 2 (4)* |
| 50-90 | 39 (78)a | 36 (90)* | 33 (73.3)a | 36 (80)* | 17 (42.5)b | 40 (72)** |
| > 90 | 11 (22)b | 0 (0)** | 10 (22.3)b | 6 (13.3)* | 19 (47.5)a | 13 (24)** |
| SCT (%) | | | | | | |
| < 15 | 22 (44)b | 40 (100)*** | 43 (95.6)b | 39 (86.7)** | 40 (100)b | 40 (72)** |
| 15-35 | 28 (56)c | 0 (0)*** | 2 (4.4)b | 6 (13.3)** | 0 (0)a | 13 (24)*** |
| > 35 | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (4)* |
| **Serum ferritin (µg/l)** | | | | | | |
| < 15 | 0 (0) | 0 (0) | 0 (0) | 12 (26.7)** | 0 (0) | 0 (0) |
| 15-150 | 50 (100) | 32 (80)* | 45 (100) | 27 (60)** | 40 (100) | 44 (80)* |
| > 150 | 0 (0) | 8 (20)** | 0 (0) | 6 (13.3)* | 0 (0) | 11 (10)** |

N: Total number of each women group; n: Subjects' number observed in each group; ARVT: Antiretroviral therapy; TIBC: Total iron binding capacity; SCT: Saturation coefficient of transferrin; *: Difference statistically significant for $p < 0.05$; a, b and c: Women groups statistically different for $p < 0.05$; **: Difference statistically significant for $p < 0.01$; ***: Difference statistically significant for $p < 0.001$.

**Components of iron status and HIV infection progression during pregnancy:** Several study women have recorded abnormal iron status (62.9 % and 92 % respectively). The results have shown that women on ARVT were more significantly exposed compared with controls (**Table 7a**). Depending on variation of iron metabolism parameters, components of iron status observed in all women were iron deficiency (ID), iron deficiency anaemia (IDA), inflammatory anaemia (IA) and inflammatory anaemia associated with iron deficiency (IA+ID).

Significant differences were reported between the two groups of HIV infected women. However, IA associated with ID has not been revealed in infected pregnant women on ARVT. In the same way, control women have not been indicated ID and IDA.

In **Table 7b**, an interaction of pregnancy and antiretroviral therapy (ARVT) was observed on different components of iron metabolism in study subjects. Thus, control women have reported low prevalence of normal iron status during three trimesters of pregnancy (46 %, 40 % and 22.5 % respectively). For abnormal iron status, ID was only recorded to second trimester of pregnancy in women on ARVT.

In addition, these women have reported IDA to first and third trimesters of pregnancy. Moreover, women on ARVT have revealed high prevalences of IA compared with controls. In contrast, control women have indicated throughout high prevalences of IA associated with ID.

**TABLE 7: REPARTITION OF IRON STATUS COMPONENTS IN STUDY INFECTED PREGNANT WOMEN**

**TABLE 7A: DISTRIBUTION OF IRON STATUS COMPONENTS ACCORDING TO TWO PREGNANT WOMEN GROUP**

| Iron status components | Infected pregnant women group | | p-values |
|---|---|---|---|
| | Control women N = 135 | HIV pregnant women/ARVT N = 140 | |
| | n (%) | n (%) | |
| Normal iron status | 50 (37.1) | 10 (8) | $6.6\ 10^{-6}$ (S) |
| Abnormal iron status | 85 (62.9) | 130 (92) | 0.02 (S) |
| Iron deficiency | 0 (0) | 6 (4) | 0.02 (S) |
| Iron deficiency anaemia | 0 (0) | 8 (6) | 0.004 (S) |
| Inflammatory anaemia | 16 (11.9) | 116 (82) | $1.7\ 10^{-14}$ (S) |
| Inflammatory anaemia + Iron deficiency | 69 (51.1) | 0 (0) | $2.2\ 10^{-16}$ (S) |

**TABLE 7B: CHANGES OF IRON STATUS COMPONENTS DURING PREGNANCY IN INFECTED PREGNANT WOMEN GROUP**

| Iron status components of infected pregnant women | Different stages of pregnancy | | | | | |
|---|---|---|---|---|---|---|
| | First | | Second | | Third | |
| | Control women N = 50 | HIV Pregnant women ARVT N = 40 | Control women N = 45 | HIV Pregnant women ARVT N = 45 | Control women N = 40 | HIV Pregnant women ARVT N = 55 |
| | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Normal iron status | 23 (46)a | 0 (0)*** | 18 (40)a | 3 (6.7)*** | 9 (22.5)b | 7 (12)* |
| Abnormal iron status | 27 (54)b | 40 (100)** | 27 (60)b | 42 (93.3)** | 31 (77.5)a | 48 (88) |
| Iron deficiency | 0 (0) | 0 (0) | 0 (0) | 6 (13.3)** | 0 (0) | 0 (0) |
| Iron deficiency anaemia | 0 (0) | 4 (10)* | 0 (0) | 0 (0) | 0 (0) | 4 (8)* |
| Inflammatory anaemia | 12 (24)a | 36 (90)*** | 3 (6.7)b | 36 (80)*** | 1 (2.5)c | 44 (80)*** |
| Inflammatory anaemia + Iron deficiency | 15 (30)c | 0 (0)*** | 24 (53.3)b | 0 (0)*** | 30 (75)a | 0 (0)*** |

N: Total number of each women group; n: Subjects' number observed in each group; a. b and c: Women groups statistically different for $p < 0.05$; **: Difference statistically significative for $p < 0.01$; ***: Difference statistically significative for $p < 0.001$

According to evolution of CD4 rates in **table 8**, no control has presented an immunodepression (CD4 < 200 cellules/µl) during first and second trimesters of pregnancy. However, women on ARVT have revealed an immunodepression throughout the pregnancy.

For the stages A and B, no study woman has indicated normal iron status to first trimester of pregnancy. In the same way, no control has reported normal iron status for second trimester of pregnancy to these stages of HIV infection. Moreover, all control women with immunodepression have not reported to third trimester of pregnancy normal iron status. Women on ARVT with ID were only in stages B and C to second trimester of pregnancy. Inflammatory anaemia more observed in women on ARVT throughout the pregnancy was significant in stages A and B. However, in these women 40 % for first and 28 % for third trimesters of pregnancy with IA were in immunodepression.

For control women with IA associated with ID, 30 % were in immunodepression (stage C) to first trimester, and 51.1 % in stage B to second trimester of pregnancy. In addition, several controls with IA associated with ID (75 %) were in stages A and B (**Table 8**).

**DISCUSSION:** The specificity of this study is to demonstrate the necessity of using antiretroviral therapy for women during pregnancy with HIV in Côte d'Ivoire. Women with HIV during pregnancy show an alteration of haematological, biochemical and immunological parameters throughout this investigation. This observation is regularly reported by several works in the world. It is even more pronounced during antiretroviral therapy in pregnant women in developing countries. The main results of this study show that the group of pregnant women infected with HIV without antiretroviral therapy, is more exposed compared with pregnant women on antiretroviral therapy.

**TABLE 8: IRON STATUS AND PROGRESSION OF HIV INFECTION**

| Iron status components and CD4 | | Different trimesters of pregnancy | | | | | |
|---|---|---|---|---|---|---|---|
| | | First | | Second | | Third | |
| | | Control women N = 50 | HIV Pregnant women ARVT N = 40 | Control women N = 45 | HIV Pregnant women ARVT N = 45 | Control women N = 40 | HIV Pregnant women ARVT N = 55 |
| CD4 (cellules/µl) | | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| < 200 | | 0 (0)b | 16(40)*** | 0 (0)b | 9 (20)*** | 16 (40)a | 15 (28)** |
| 200-499 | | 0 (0)b | 16(40)*** | 43 (95.6)a | 27 (60)** | 24 (60)c | 31 (56)** |
| ≥ 500 | | 50 (100)c | 8 (20)*** | 2 (4.4)b | 9 (20)** | 0 (0)a | 9 (16)** |
| **Iron status** | **Stages of infection** | | | | | | |
| NIS | A | 0 (0)b | 0 (0) | 17 (37.8)a | 0 (0) *** | 5 (12.5)c | 0 (0)** |
| | B | 0 (0)b | 0 (0) | 1 (2.2)b | 0 (0) | 4 (10)a | 4 (8) |
| | C | 23 (46)a | 0 (0)*** | 0 (0)b | 3 (6.7)* | 0 (0)b | 2 (4)* |
| ID | A | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | B | 0 (0) | 0 (0) | 0 (0) | 3 (6.7)* | 0 (0) | 0 (0) |
| | C | 0 (0) | 0 (0) | 0 (0) | 3 (6.7)* | 0 (0) | 0 (0) |
| IDA | A | 0 (0) | 4 (10)** | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | B | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 4 (8)* |
| | C | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| IA | A | 0 (0)b | 4 (10) ** | 3 (6.7)a | 9 (20)** | 1 (2.5)c | 4 (8)* |
| | B | 0 (0) | 16(40) *** | 0 (0) | 24 (53.3) | 0 (0) | 24 (44)*** |
| | C | 12 (24)a | 16(40)* | 0 (0)b | 3 (6.7)* | 0 (0)b | 15 (28)*** |
| IA + ID | A | 0 (0)b | 0 (0) | 0 (0)b | 0 (0) | 10 (25)a | 0 (0)*** |
| | B | 0 (0)b | 0 (0) | 23 (51.1)a | 0 (0)*** | 20 (50)a | 0 (0)*** |
| | C | 15 (30)b | 0 (0)*** | 1 (2.2)a | 0 (0) | 0 (0)a | 0 (0) |

N: Total number of each women group; n: Subjects' number observed in each group; a. b and c: Women groups statistically different for $p < 0.05$; **: Difference statistically significative for $p < 0.01$; ***: Difference statistically significative for $p < 0.001$; NIS: Normal Iron Status; ID: Iron Deficiency; IDA: Iron Deficiency Anaemia; IA: Inflammatory Anaemia; IA+ID: Inflammatory Anaemia + Iron Deficiency; A (≥ 500 cellules/µl) ; B (200-499 cellules/µl); C (< 200 cellules/µl).

Indeed, assessment of biological indicators of iron metabolism shows that more than half of HIV infected pregnant women without antiretroviral treatment showed IA associated with ID. No IDA is observed in these subjects. Installation mechanism of anaemia is a dynamic concept. This is carried out using several steps and is characteristic of type of anaemia. In developing countries, main observed types of anaemia are nutritional and infectious origins. Anaemia due to iron deficiency follows three stages [28]:

First, simple depletion of iron reserves without deficiency of erythropoiesis is characterized by low serum ferritin below standards (below 15 mg/l). Then, depletion with deficiency of erythropoiesis is associated with a decrease in saturation coefficient of transferrin, increase in transferrin and total iron binding capacity, a decrease in serum iron and erythrocyte parameters. The last stage corresponds to IDA where the hemoglobin level falls below the threshold [29].

The main raison of iron deficiency is the insufficient of bioavailability's iron in the diet of developing countries' population. In addition, iron deficiency is also caused by iron needs during pregnancy. This study reveals that women were concerned by ID during pregnancy. This result was previously reported in Abidjan with followed women during pregnancy [30].

In addition, the previous study has indicated a high prevalence of IDA in pregnant women. In contrast, our study population shows more inflammatory anaemia. This anaemia is resulted in inflammatory and infectious syndromes. HIV infection causes inflammation in subjects. This inflammation has an impact on iron metabolism by cytokines, interferons and iron sequestration by macrophages. This whole set disturbs the proper functioning of iron stores (ferritin), transport protein (transferrin) and erythropoietin. In fact, transcription of the erythropoietin gene is facilitated by hypoxia inducible factor (HIF-1).

Erythropoietin acts through its receptor to exert its proliferative, differentiator and anti-apoptotic effects on erythroid precursors. Gamma interferon, inflammatory cytokines interleukin-1 (IL-1) and TNF-alpha (TNF-a) inhibit the expression of erythropoietin gene, formation of erythroid colony and function (IFN-g) of erythropoietin receptor. This leads to poor erythropoiesis with an insufficient of synthesis in red blood cells. Therefore, blood cell production is weak with an impact on haematological parameters of iron status. In this study, all haematological parameters are modified during pregnancy in subjects.

Indeed, a poor unwinding of erythropoiesis causing a defective synthesis of red blood cells, occurs in the body. This insufficiency of blood cell production has an effect on the blood parameters of iron status. In the event of our research, red blood cells, hematocrit, hemoglobin, MCV (pregnant women without ART), MCH and MCHC (pregnant women on ARVT) are modified. The Changes in hematological parameters through an inadequate of erythropoiesis can be explained by the disorder of iron metabolism from sequestration by macrophages of iron released through hemolysis. This sequestration of iron causes difficulty of its mobilization from reserves. This deficit of movement of iron in body leads to:

- A static state or high iron stores (normal or high ferritin);
- A decrease of plasma transferrin (iron transport protein) due to its hypercatabolism in the inflammatory focus, on the other hand the decrease in its synthesis (iron stores are full);
- A reactive increase in number of mitoses liable for microcytosis [31].

These findings are similar to those of our study. Indeed, the mean values of serum ferritin in both groups of pregnant women infected with HIV are normal. Moreover, high prevalence of microcytosis and hypochromia are reported in the group of pregnant women without antiretroviral therapy. In contrast, this study revealed normal concentrations of serum transferrin in all selected women.

Also very few pregnant women infected with HIV of works indicate a decrease in serum transferrin. Inflammatory anaemia may to know two phases of evolution:

- Anaemia is initially normocytic normochromic aregenerative.
- Inflammation persisting, anaemia may be hypochromic and microcytic [32, 33].

This could explain the high rates of hypochromic microcytic anemia (HMA) and normochromic normocytic anaemia (NNA) in selected subjects of study. Furthermore, a high prevalence of macrocytosis is observed only in pregnant women infected with HIV on ART. This is contrary of all events that occur during a change of iron metabolism in HIV infection.

This macrocytosis could be justified by non-observance of recommended folic acid during pregnancy. According to work of Spanish researchers, a significant macrocytosis is observed in HIV subjects and without antiretroviral therapy, which is against to our findings [34]. Difference in physiological states among subjects of the two studies could explain these opposite results. Moreover, a large proportion of control pregnant women indicate high values of transferrin that leads to inflammatory anaemia associated with iron deficiency in these subjects. This result is similar to that reported in South African with 23.9 % against 24.9 % in ours with high concentrations of transferrin [35].

Our study reveals that in antiretroviral therapy in women during pregnancy with HIV infection, altered metabolic pathways of iron is observed. Similar results were reported in HIV infected pregnant women with high antiretroviral therapy in Latin America and caraïbes with a prevalence of anaemia of 12.2 % against 62.2 % (Pregnant Women without ARVT) and 71.4 % (pregnant women on ARVT) [36].

In the event of our investigation, prevalence of anemia is higher than that indicated in the Latin American and caraïbean. The interaction between antiretroviral therapy and pregnancy on biological indicators of iron metabolism assessment has an impact on haematological parameters, iron, transferrin, TIBC and SCT in first trimester and third trimester. However, this interaction is more active throughout pregnancy (in all three trimesters) on iron stores (ferritin), inflammatory anaemia and inflammatory anaemia associated with iron deficiency.

These results are contrary to those reported in non HIV infected pregnant women in Abidjan [30]. For these authors, iron metabolism is altered in the last trimester of pregnancy. The observed type of anaemia is of nutritional origin. This could be explained by infectious and inflammatory syndrome caused by HIV infection in pregnant women.

In addition, HIV infected pregnant women on ARVT indicate inflammatory anaemia most important in stage A of HIV infection during the last two trimesters of pregnancy. In contrast, infected pregnant women and devoid of antiretroviral therapy reveal inflammatory anaemia with iron deficiency in early pregnancy at stage C of HIV infection.

The evolution of CD4 count in pregnant women during antiretroviral therapy is increasing [37]. This observation is similar to that reported in our research on pregnant women with ARVT. However, it is contrary to infected pregnant women without antiretroviral treatment. This is revealed in control pregnant women of our investigation. Studies also indicated low rates of pregnant women [38, 39]. In addition, altered iron status in infected pregnant women in their entirety was observed during other research study [40]. Conversely, a work revealed that the status is not based on the progression of HIV infection in pregnant women [41].

Antiretroviral treatment would reduce deficiency and overload of some micronutrients such as selenium, zinc, copper and even iron. The work over four years of antiretroviral therapy in subjects infected with HIV showed that a decrease of iron deficiency (< 6 µmol/l) from 19 % to 13 %, selenium (< 60 mg/l), 77 % to 10 % and copper overload (> 140 mg/dl) from 9% to 43 % among 44 HIV infected subjects on high antiretroviral therapy [8].

Antiretroviral therapy depresses prevalence of opportunistic gastrointestinal diseases and severe gastroenteritis. These pathologies affect the absorption of micronutrients. However, several medications against HIV (NRTI3) can inhibit the replication of mitochondrial DNA and cause vomiting and diarrhea that may reduce absorption or increase losses of several micronutrients. This could also explain the degradation of iron metabolism in women in our study. Nutrition and pharmacology of antiretrovirals are actually related as this study so well indicates [42, 43, 44].

**CONCLUSION:** Antiretroviral therapy and pregnancy disrupted various biological indicators of iron metabolism assessment in all pregnant women with HIV. Infected pregnant women without antiretroviral therapy are more changes of iron status parameters compared with those who are on this medication. All components of the iron metabolic pathways are reported in this work. It is iron deficiency, iron deficiency anaemia, inflammatory anaemia and inflammatory anaemia associated with iron deficiency.

The interaction between antiretroviral therapy and pregnancy on biological indicators of iron metabolism has an impact on haematological parameters, iron, transferrin, TIBC and SCT in first trimester and third trimester. However, this interaction is more active throughout pregnancy (all three trimesters) of iron stores (ferritin), inflammatory anaemia and inflammatory anaemia with iron deficiency. Pregnant women on ARVT indicate high rates of inflammatory anaemia at last trimester of pregnancy in stage C (≥ 500 cells/µl) of the HIV infection.

However, control women have a high prevalence of inflammatory anaemia with iron deficiency in early pregnancy stage C (≤ 200 cells/µl) of HIV infection. Iron deficiency and iron deficiency anaemia are observed only in pregnant women on ARVT. The possible reasons for these changes in iron status of pregnant women infected with HIV in Abidjan are pregnancy and antiretroviral medication.

To better appreciate the different risk, it would be appropriate to study the influence of HIV, antiretroviral therapy and the three trimesters of pregnancy on iron metabolism in pregnant women in Abidjan.

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## REFERENCES :


1. WHO: Programme VIH/SIDA. Renforcer et étendre les systèmes de santé pour lutter contre le VIH/SIDA: médicaments antirétroviraux pour traiter la femme enceinte et prévenir l'infection à VIH chez l'enfant; vers un accès universel. Recommandations pour une approche de santé publique. Génève, ONUSIDA, 2006; 96. http://whqlibdoc.who.int/publications/2007/9789242594669_fre.pdf accessed 28/04/2012
2. Carra A and Amin J: Efficacy and tolerability of initial antiretroviral therapy: a systematic review. AIDS 2009; 23:343–353
3. WHO: La stratégie mondiale du secteur de la santé sur le VIH/SIDA 2011-2015. Geneva, UNAIDS 2010; 52. http://whqlibdoc.who.int/publications/2011/9789242501650_fre.pdf, Accessed 28/04/2012
4. Mintz M: Carnitine in human immunodeficiency virus type 1 infection/acquired immune deficiency syndrome. Journal of Child Neurology 10(Suppl), 1995; 2S40–2S44.
5. Shet A, Mehta S, Rajagopalan N, Dinakar C, Ramesh E, Samuel NM, Indumathi CK, Fawzi WW and Kurpad AV: Anemia and growth failure among HIV-infected children in India: a retrospective analysis. BMC Pediatrics 2009; 9:37 doi:10.1186/1471-2431-9-37.
6. Carr A, Miller J, Law M and Cooper DA: A syndrome of lipoatrophy, lactic acidaemia and liver dysfunction associated with HIV nucleoside analogue therapy: contribution to protease inhibitor-related lipodystrophy syndrome. AIDS 2000; 14: F25–F32.
7. Bogden JD, Baker H, Frank O, Perez G, Kemp F, Bruening K and Louria D: Micronutrient status and human immunodeficiency virus (HIV) infection. Annals of the New York Academy of Sciences 1990; 587: 189–195.
8. Rousseau MC, Molines C, Moreau J and Delmont J: Influence of highly active antiretroviral therapy on micronutrient profiles in HIV-infected patients. Annals of Nutrition and Metabolism 2000; 44(5-6): 212-6.
9. Ndeezi G, Tumwine JK, Bolann BJ, Ndugwa CM and Tylleskär T: Zinc status in HIV infected Ugandan children aged 1-5 years: a cross sectional baseline survey. BMC Pediatrics 2010; 10:68 http://www.biomedcentral.com/1471-2431/10/68
10. McIntyre J: Use of antiretrovirals during pregnancy and breastfeeding in low-income and middle-income countries. Current Opinion in HIV and AIDS 2010; 5:48–53
11. Edmonds A, Yotebieng M, Lusiama J, Matumona Y, Kitetele F, Napravnik S, Cole SR, Van Rie A and Behets F: The Effect of Highly Active Antiretroviral Therapy on the Survival of HIV-Infected Children in a Resource-Deprived Setting: A Cohort Study. PLoS Medicine 2011; 8(6): e1001044. doi:10.1371/journal.pmed.1001044
12. Musoke PM and Fergusson P: Severe malnutrition and metabolic complications of HIV-infected children in the antiretroviral era: clinical care and management in resource-limited settings. American Journal of Clinical Nutrition 2011; 94: 1667S-1676S
13. Toure S, Kouadio B, Seyler C, Traore M, Dakoury-Dogbo N and Duvignac J: Rapid scaling-up of antiretroviral therapy in 10000 adults in Cote d'Ivoire: 2-year outcomes and determinants. AIDS 2008; 22:873–882.
14. Ouyanga DW, Broglyb SB, Ming L, Shapirob DE, Hershowd RC, Frenche AL, Leightyc RM, Thompsonc B and Tuomala RE: Lack of increased hepatotoxicity in HIV-infected pregnant women receiving nevirapine compared with other antiretrovirals AIDS 2010; 24:109–114
15. Antelman G, Msamanga GI, Spiegelman D, Urassa EJN, Narh R, Hunter DJ and Fawzi WW Nutritional Factors and Infectious Disease Contribute to Anemia among Pregnant Women with Human Immunodeficiency Virus in Tanzania. Journal of Nutrition 2000; 130: 1950–1957.
16. Beaton GH: Iron needs during pregnancy: do we need to rethink our targets? American Journal of Clinical Nutrition 2000; 72: 265S-271S.
17. Dreyfuss M, Msamanga GI, Spiegelman D, Hunter DJ, Urassa EJN, Hertzmark E and Fawzi WW: Determinants of low birth weight among HIV-infected pregnant women in Tanzania. American Journal of Clinical Nutrition 2001; 74:814–26.
18. Szylda EG, Warleya EM, Freimanisf L, Goninf R, Cahnb PE, Calvetc GA, Duarted G, Meloe VH and Jennifer S: Maternal antiretroviral drugs during pregnancy and infant low birth weight and preterm birth Readg for the NISDI Perinatal Study Group AIDS.2006; 20:2345–2353
19. Moh R, Danel C, Sorho S, Sauvageot D, Anzian A, Minga A, Gomis OB, Konga C, Inwoley A and Gabillard D: Haematological changes in adults receiving a zidovudine-containing HAART regimen in combination with cotrimoxazole in Cote d'Ivoire. Antiviral Therapy 2005; 10:615-624.
20. WHO (World Health Organisation): HIV/AIDS Programme/Strengthening health services to fight HIV/AIDS. Antiretroviral therapy for HIV infection in adults and adolescents: recommendations for a public health approach. Geneve UNAIDS, Switzerland, 2010; 156. http://whqlibdoc.who.int/publications/2010/9789241599764_eng.pdf, accessed 28/04/2012
21. UNAIDS: Inter-Agency Standing Committee Task Force on HIV. Guidelines for addressing HIV in humanitarian settings. Geneva, UNAIDS 2010; 68 p. http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2010/jc1767_iasc_doc_en.pdf consulté le 28/04/2012
22. Vernet M, Corberand J and David V: Algorithmes de prescription recommandés pour le diagnostic d'un déficit et d'une surcharge en fer. Annale de Biologie Clinique (Paris) 2001; 59: 149-55.
23. Institute of Medecine (IOM/USA): Comittte on nutritional status during pregnancy and lactation. Nutrition during pregnancy: weight gain and nutrient supplements. Washington DC. National Academy Press 1990.
24. UNICEF/UNU/WHO: Iron deficiency anemia: assessment, prevention, and control. WHO/NHD/01.3 Geneva, Switzerland: WHO 2001.
25. Duport N, Preziosi P, Boutron-Ruanlt MC, Bertrais S, Galan P, Favier A, Lafond JL and Hercberg S: Consequences of iron depletion on health in menstruating women. European Journal of Clinical Nutrition 2003; 57(9): 1169–1175.

26. SNDLF: Société de Nutrition et de Diététique de Langue Française, 2001. Anémies nutritionnelles (SNDLF). Cahier de Nutrition et Diététique 2001; 36 (Hors série) : 76-81.
27. Statsoft: Statistica (Data Analysis Software System). Version 7.1 2005; available at www. Statsoft.com
28. Ihaka R and Gentleman R: R: a language for data analysis and graphics. J. of computation. graphic and statistic 1996; 5:299-314.
29. Herbecg S, Galan P, Prual A and Prezioi P: Epidémiologie de la déficience en fer et de l'anémie ferriprive dans la population française. Annale de Biologie Clinique (Paris) 1998; 56(1): 49–52.
30. Bleyere NM, Ekaza-Joulia D, Yapo AP, N'guessan BB, Neil Cathy AM, Vanga OM, Koné M and Ehilé EE: Heterogeneity of iron status in women during pregnancy in Cote d'Ivoire. Annale de Biologie Clinique (Paris) 2007; 65 (5): 525-532.
31. Tsiakalos A, Kordossis T, Ziakas PD, Kontos AN, Kyriaki D and Sipras NV: Circulating antibodies to endogenous erythropoietin and risk for hiv-1 related anemia. Journal of infection 2009; 60(3): 238-43
32. Beisel WR: History of nutritional immunology: introduction and overview. Journal Nutrition 1992; 122: 591–6.
33. Boelaert JR, Weinberg GA and Weinberg ED: Altered iron metabolism in HIV infection: mechanisms, possible consequences, and proposals for management. Infectious agents and disease 1996; 5(1): 36-46.
34. Remacha AF, Cadafalch J, Sarda P, Barcelo M and Fuster M: Vitamin B-12 metabolism in HIV-infected patients in the age of highly active antiretroviral therapy: role of homocysteine in assessing vitamin B-12 status. American Journal of Clinical Nutrition 2003; 77:420–4.
35. Walsh CM, Hattingh Z, Veldman FJ and Bester CJ: Iron status and anaemia of chronic disease in HIV-infected African women in Mangaung, Bloemfontein. SA Family Practice 2010; 55-59
36. Kurz K, Seifert M, Sarcletti M, Fuchs D, Weiss G and Zangerle R: Iron metabolic changes and immune activation in patients with HIV-1 infection before and after one year of effective antiretroviral therapy: AIDS-XVIII International AIDS Conference: 2010; Abstract no. CDB0042.
37. Batterham M and Garsia R: A comparison of megestrol acetate, nandrolone decanoate and dietary counselling for HIV associated weight loss. International journal of andrology 2001; 24(4), 232-40.
38. Loko MA, Toure S, Dakoury-Dogbo N, Gabillard D, Leroy V and Anglaret X: Decreasing incidence of pregnancy by decreasing CD4 cell count in HIV-infected women in Cote d'Ivoire: a 7-year cohort study. AIDS 2005; 19:443–445.
39. Smith CJ, Sabin CA, Lampe FC, Shah S, Tyrer M and Youle MS: The relationship between CD4 cell count nadirs and the toxicity profiles of antiretroviral regimens. Antiviral Therapy 2005; 10:459–467.
40. Weinberg GA, Friis H, Boelaert JR and Weinberg ED: Iron status and the severity of HIV infection among pregnant women [letter]. Clinical Infectious Disease 2001; 33:2098–9.
41. Semba RD, Taha ET, Kumwenda N, Mtimavalye L, Broadhead R, Miotti PG and Chiphangwi JD: Iron status and indicators of human immunodeficiency virus disease severity among pregnant women in Malawi. Clinical Infectious Disease 2001;32: 1496–9.
42. Baum MK, Shor-Posner G and Lu Y: Micronutrients and HIV-1 disease progression. AIDS 1995; 9:1051-1056.
43. Drain PK, Kupka R, Mugusi F and Fawzi WW: Micronutrients in HIV-positive persons receiving highly active antiretroviral therapy. American Journal of Clinical Nutrition 2007; 85:333-45.
44. Raiten DJ: Nutrition and pharmacology: general principles and implications for HIV**.** American Journal of Clinical Nutrition 2011; 94: 1667S-1676S.


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