

Study on the Biochemical Alterations in People with Human Immunodeficiency Virus Infection both before and after Antiretroviral Therapy

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Abstract:

Biochemical changes in people infected with the human immunodeficiency virus before and after treatment with antiretroviral drugs are described in this study. Antiretroviral therapy (ART) improves the health and lifespan of people living with HIV-1, but it also raises the danger of metabolic abnormalities in some patients. This study consisted a group of people with HIV who had never taken ART before for a few months to see if their nutrition or the way the medicine worked, changed. The goal of study is to evaluate blood counts and other biochemical markers in HIV patients receiving antiretroviral medication. A regular screening of HIV on antiretroviral medication is necessary to identify individuals in need of nutritional care because the improvement in nutritional status appears to be a glacial. A total of 9,418 HIV patients with ART failure among 2004 and 2016 were included in this retrospective analysis. Age, CD4 count, viral load, hyperglycemia, creatinine & triglyceride levels were acquired from EHR databases to monitor patients' progress.

Keywords: HIV, ART, antiretroviral, changes, people, antiretroviral drugs

1. INTRODUCTION

HIV-1 infection is a leading global health issues and the pandemic's effects on humanity have grown exponentially since AIDS was first recognized. It is estimated that 37.7 million people will have HIV-1 infection by the year 2020. From 2007 to 2020, the region of India accounted for 36,218 of the total 381,793 new cases in India. In terms of monitoring supplementary testing and genotyping HIV-1 strains to assess ART efficacy, the public health system in India is among the most effective in the world. Treatment with ART delays disease progression, increases longevity, enhances quality of life, and decreases susceptibility to opportunistic infections [1]. By June 2021, it is expected that 28.2 million people, or globally, 73% of all HIV-1 carriers are women, would have access to ART (PLHIV). Although ART is accessible at no cost through the Indian government health care system, the success of a patient's medication depends on several elements, including the patient's adherence to the treatment plan, which is affected by factors such as the patient's choice of drugs, the frequency with which antiretroviral are administered, the patient's psychological and social circumstances, as well as the impacts of the patient's present diet, may interfere with or be dependent on the effectiveness of the treatment. When ART is not used to combat the increased metabolic demands of HIV-1 infection, cachexia develops [2]. Consumption and use of nutrients determine an individual's nutritional state; insufficiency in either can promote

illness and speed up the onset of AIDS. Malnutrition and a decline in clinical status are associated with HIV-1 infection and ART due to alterations in metabolism and the gastrointestinal tract [3]. Hence, PLHIV can benefit from improved therapeutic & immune system responses [4] if they are provided with a sufficient dietary treatment. While antiretroviral therapy (ART) is effective in reversing the immunological decline brought on by HIV infection, a lack of calories may reduce its effectiveness [5]. HIV treatment improves immune function & reduces viral load, but it may raise the risk of cardiovascular and kidney diseases [6]. The introduction of ART led to a dramatic rise in PLHIV survival rates, which had a profound effect on their quality of life. Sugar, lipid, and dyslipidemia abnormalities were also found [7]. The strong affinity of nucleoside analogue reverse transcriptase (NRTI) inhibitors for HIV-1 reverse transcriptase causes metabolic acidosis [8]. The emergence of dyslipidemia is more frequently linked to the use of protease inhibitors (IP) [9]. So, it is crucial to determine PLHIV's nutritional condition before initiating ART in order to identify those who will benefit from nutritional therapy as an adjunct to ART. Furthermore, by periodically monitoring patients throughout therapy, Potential dietary shifts associated with ART-related metabolic diseases may be isolated.

1.1 PSYCHOSOCIAL FACTORS AND INFERTILITY IN HIV

Patients infected with HIV may have varying reproductive results based on their individual psychological traits. When someone receives a new HIV diagnosis, they may choose to reduce their sexual activity. Pregnancy & birth rates seem to be dropping among HIV-positive women. Despite these efforts, Many HIV-positive women still engage in risky activities and become pregnant unintentionally. Because of this, women with HIV are also more prone to have abortions. With a new HIV diagnosis, the pregnancy termination rate in Britain and Ireland rises from 3.5 to 6.3 per 100 women. This trend holds true across all age groups and ethnicities. More than double the national average, 47% of pregnant women in India ended their pregnancies after receiving an HIV diagnosis. The difficulties of pregnancy, delivery & motherhood in the setting of HIV infection may lead some HIV-positive women to choose abortion. Several studies have found that the rate of elective abortion among HIV-positive women has decreased with the widespread implementation of HAART in clinical exercise. Townsend et al. [10] found that the termination rate in the UK and Ireland plummeted from 29.6% in 1990-1993 to 3.4% in 2004-2006. As zidovudine (AZT) prophylaxis was introduced in India, the percentage of pregnancies that ended in termination dropped from 59.4 percent to 37.5 percent. Based on data from a U.S. cohort, found that HAART users had a 33% lower risk of having an elective termination of pregnancy compared to women not receiving therapy (OR, 0.33; 95% CI, 0.17-0.67). For HIV-positive women, having an unanticipated pregnancy, a low CD4 count, or a current partner who is HIV-positive all significantly increased the likelihood of an elective termination [11]. Widespread use of HAART has enhanced the likelihood that HIV-1-infected women can overcome the biological subfertility caused by the virus itself through a combination of behavioural changes and improvements in general health and immunological function. A more optimistic outlook on the efficacy of HAART has been linked to increased sexual desire and activity. High levels of optimism on the HAART scale were seen among women who

intended to increase their family size as compared to those who did not. Unprotected sexual activity was associated with considerably higher HAART optimism levels among sexually active women than among abstaining or protected sexual activity [12]. Even though these patients' behaviours may make sense, further direct studies examining the effects of HAART on reproductive competence and behaviour are required.

1.2 MALE INFERTILITY AND HIV/AIDS

HIV-1 infected men have drastically decreased sperm parameters that indicate infertility. Patients with advanced AIDS may be less fertile than HIV-1-infected men who are in better condition, according to a study that found a positive correlation between sperm quality and CD4 count [13]. There may be a connection between oligospermia and teratozoospermia in HIV-1-infected men & the increased prevalence of orchitis, hypogonadism, and leukospermia. Analysis of sperm morphological damage using atomic force microscopy revealed that HAART, and not the HIV-1 virus, was to blame and topography among HIV/AIDS patients. As compared to previous studies, in which AZT therapy had no negative effect on sperm, these ultrastructural findings are counterintuitive. According to the most recent studies, HAART may considerably reduce the total sperm count, progressive motility & post-preparation sperm count, while increasing the frequency of aberrant sperm types. HIV-infected men face major challenges such as hypogonadism, diminished libido, and impotence. It is predicted that 60% of men with severe illness may experience erectile and ejaculatory dysfunction. PDE5 inhibitors for the cure for erectile dysfunction should be used with caution by individuals taking protease inhibitors because both drug families are metabolised via cytochrome P450 3A4. To reduce the possibility of unwanted side effects like priapism, it is recommended to begin treatment with the smallest effective dose of PDE5 inhibitor.

2. REVIEW OF LITERATURE

Grulich et al (2015) discussed the study on the epidemiology of malignancies associated with HIV infection and subsequent organ transplantation. This study improves the understanding of how HIV patients and those who have received solid organ transplants fare in terms of cancer risk in relation to immune weakness. Kaposi sarcoma (KS) & non-Hodgkin lymphoma (NHL) are two of the many cancers that have been connected to immunosuppression. Both KS and NHL are associated with human herpes virus 8 (HHV8) and Epstein Barr Virus (EBV). Another common kind of cancer in transplant recipients is squamous cell carcinoma (SCC) of the skin, and it's thought that this is due to the immunosuppressant drugs themselves having carcinogenic effects. There have been significant recent shifts in the incidence of cancer in these two populations due to epidemiological and clinical factors.

Da Cunha et al. (2015) discussed the investigation on the impact of old and new drugs on the lipid metabolism of individuals with human immunodeficiency virus infection during antiretroviral therapy. The development of HAART in the 1990s gave HIV-positive individuals a second chance at a healthy life. In individuals infected with HIV-1, HAART has been shown to significantly decrease mortality and morbidity rates, leading to an improved

and prolonged quality of life for these individuals. The effects of lipid metabolism include lipodystrophy, insulin resistance, central obesity, dyslipidemia, an increase in the risk of cardiovascular disease & even an enhanced risk of atherosclerosis; have been shown in the laboratory and in clinical practise to be induced by HAART.

Menéndez-Arias et al. (2014) performed a study on antiretroviral therapy & medication resistance in infection with HIV type 2. One to two million people is infected with HIV-2 globally, with the highest prevalence's occurring in West African countries. Western Europe, Asia, & North America are not the only regions where HIV-2 has been documented. The reduced viremia in HIV-2 patients is one reason why the virus is less likely to be transmitted than HIV-1. Many antiretroviral medications that are effective against HIV-1, including non-nucleoside RT inhibitors, various protease inhibitors, or the fusion inhibitor enfuvirtide, are ineffective against HIV-2. The rate of resistance selection may be an area in which HIV-1 and HIV-2 selected. This study summarizes anti-HIV-2 medications and discusses the mutation processes that lead to drug resistance.

Fitting et al (2013) discussed the study of Learning and memory problems are accompanied with synaptic disruption in the hippocampus in HIV-1 Tat transgenic mice. HIV type-1 infection is still commonly manifested clinically by memory problems and other neurocognitive disorders (HAND), such as AIDS dementia. The relationships between the organisation and function of pyramidal cornuammonis 1 (CA1) neurons in the hippocampus were investigated using a glial fibrillary acidic protein-driven, doxycycline-inducible HIV type-1 transactivator for transcription (Tat) transgenic mouse model. Particularly, we employed morphologic, electrical, or behavioural (Morris water maze, fear-conditioning) approaches. In astrocytes, inducing transactivator for transcription led to the appearance of multiple types of inclusions inside the distal cytoplasmic processes, including lysosomes, autophagic vacuoles & lamellar bodies.

Frantz et al (2013) explained the study on the levels of physical activity among Rwandans using very aggressive antiretroviral therapy & living with HIV/acquired immunodeficiency syndrome. High-dose antiretroviral therapy (HAART) is becoming more widely available to HIV patients in Rwanda. Physical activity is one of the recommended preventative strategies for these problems. The goal of this study is to characterise the anthropometrics and physical activity levels of HAART recipients in Kigali, Rwanda. A descriptive, quantitative, cross-sectional design was used for this investigation. During the course of two years, 407 patients who visited the clinics filled out a systematic, self-administered questionnaire to assess their current levels of physical activity and its correlation with their anthropometric profiles. Almost 70% of the participants did not get enough exercise, and 41% were overweight or obese. Barriers to physical activity included a lack of motivation, a lack of time & a concern of making the sickness worse.

Pfefferbaum et al. (2012) conducted a study on the impacts of AIDS, alcoholism, and ageing on regional brain structural dysmorphology in HIV infection. In addition to HIV infection, alcohol abuse compromises brain structure and function. There were 342 men and women who took part in the study: 110 alcoholics, 59 persons with HIV infection, 65 people having

HIV infection & alcoholism, or 108 healthy controls. Twenty tissue locations and five ventricular and sulcal areas had their volumes quantified and the results were shown as Z-scores that were adjusted for intracranial capacity and age. CD4 cell-count nadir, clinical stage, history of AIDS-defining events, age at infection, & current age were all characteristics related to HIV illness that were associated with larger volume abnormalities. The structural integrity of people's brains was severely impacted by HIV infection, alcoholism, and AIDS.

Lazzaretti et al (2012) explained the investigation HIV type 1 infected individuals: Nutritional intervention protects dyslipidemia associated with highly active antiretroviral therapy: a randomised trial. The goal of this study was to determine whether or not dietary intervention improved blood lipids in newly diagnosed HIV-1 patients beginning HAART. 83 HIV-1-infected patients who were HAART-naïve were split into two groups for a 12-month period: the diet group (n = 43) & the control group (n = 40). The percentage of calories consumed as fat decreased from 31.7 to 21.3 on the diet, while it remained constant in the control group. In the control group, cholesterol levels rose from 15129 to 19033 mg/dl, while in the diet group, they remained stable at 10631 mg/dl. Dyslipidemia caused by HAART can be avoided with proper dietary management in HIV-1-positive people who have never been treated.

Kushnir et al (2011) conducted a study of infertility, the HIV and the acquired immunodeficiency syndrome: new issues in the era of highly potent antiretroviral. This study is aimed at evaluating how HIV/AIDS and its therapy, antiretroviral drugs, affect fertility. Physiological alterations in the reproductive system have been related to HIV infection and subsequent infertility. Patients living with HIV may experience complications in conceiving a child due to psychological and social reasons. Health care providers are becoming increasingly concerned about the future reproductive ambitions of young HIV-infected patients, but little data exist on how HIV & its treatments affect fertility & pregnancy results for these people.

Makinson et al. (2010) presented the research on interactions between cytotoxic chemotherapy & antiretroviral therapy in HIV-positive lung cancer patients. Combining antiretroviral therapy (CART) & lung cancer therapy is between combination antiretroviral therapy (CART) & lung cancer therapy are a new clinical problem. In addition, emerging research reveals that HIV-positive individuals have a greater relative risk of acquiring lung cancer than the overall population. Protease inhibitors/ritonavir may have fatal interactions with taxanes, vinca alkaloids, and the anilinoquinazolinesterlotinib, gefitinib, and irinotecan, as shown by pharmacokinetic data and clinical instances. Clinical and antiretroviral histories, as well as the ability to forecast adverse events and interactions, play a role in the multidisciplinary decision that must be made when determining the optimal combination of chemotherapy & CART for HIV-infected patients with lung cancer.

3. METHODOLOGY

Electronic health records (EHRs) from Indian hospitals were mined for data. This database includes information on 92,957 HIV, or about 14% of the total HIV population in the India.

The age, sex, marital status, route of HIV infection, ART regimen, grounds for drug withdrawal, CD4 count & VL, GLU, creatinine (Cr), TG, PLT, AST & ALT values of a patient are only some of the demographics that are routinely recorded in electronic health records and HIV case study databases. This analysis includes 9,418 HIV patients; sample characteristics are included in Tables 1 & Figure 1. From 2004 to 2016, the study examined at the clinical examination markers for HIV/AIDS cases that ended in drug withdrawal or death after ART.

4. RESULT

Table 1: Biochemical indicator analysis of HIV patients

Variables	Total	Group 1	Group 2	P- value
Age (year)	9,418 (41.3 ± 13.4)	5,218 (43.1 ± 14.6)	4,200 (39.1 ± 11.4)	<0.001
Time interval (month)	9,418 (3.7 [24.4])	5,218 (1.2 [4.4])	4,200 (27.4 [50.9])	<0.001
CD4 count (cells/ μ l)b	9,257 (175.0 [205.0])	5,119 (153.0 [215.0])	4,138 (200.0 [183.0])	<0.001
VL (copies/ml)b	909 (220.0 [4100.0])	522 (298.5 [3600.0])	387 (147.0 [4977.0])	0.933
ALT (U/L)b	5,679 (30.0 [32.0])	3,013 (29.0 [32.0])	2,666 (32.0 [32.1])	<0.001
AST (U/L)b	5,532 (35.0 [31.0])	2,943 (34.0 [31.0])	2,589 (36.1 [30.0])	<0.001
GLU (mmol/L)b	2,092 (5.2 ± 1.7)	1,064 (5.3 ± 1.9)	1,028 (5.1 ± 1.4)	0.046
TG (mmol/L)b	1,028 (1.4 [0.9])	579 (1.5 [1.0])	449 (1.4 [0.8])	0.002
TC (mmol/L)b	1,025 (4.1 ± 1.2)	578 (4.1 ± 1.2)	447 (4.0 ± 1.1)	0.085
Cr (μ mol/L)b	2,566 (73.0 [28.2])	1320 (72.0 [28.1])	1,246 (74.0 [28.5])	0.0011
Platelet ($\times 10^9$ /L)b	5,354 (167.0 [109.0])	2,896 (173.0 [117.0])	2,548 (160.0 [103.0])	<0.001
Serum amylase (U/L)b	1,641 (75.2 [49.5])	795 (73.0 [52.0])	846 (78.0 [48.0])	0.062

Abbreviations: VL= viral load; ALT= Alanine transaminase; AST= Aspartate aminotransferase; GLU: Glucose; TG: Triglyceride; TC: Total cholesterol; Cr: Creatinin

Group 1 had lower CD4 counts than Group 2 ($P < 0.001$), with a median CD4 count of 175.0 cells/l (IQR, 77.0 - 282.0). When comparing the two groups, **Table 1** shows that Group 1 had significantly lower levels of biochemical indicators such as ALT, AST, Cr & haemoglobin. By comparing Group 1 and Group 2, Group 1 had greater GLU; TG & PLT levels ($P > 0.05$). Comparing the two groups, there was no discernible difference in serum amylase or TC levels ($P > 0.05$).

Repeated measurement data covariance analysis examining the impact of baseline information on indicator shifts over ART confirmed these findings. Figure of ART confirmed these findings & Figure 1 depicts the evolution of the major biochemical indicators as a function of ART treatment length. There was no statistically significant interaction between group & time for the other parameters (CD4, ALT, GLU, TG, Cr, PLT, & serum amylase; $P > 0.05$).

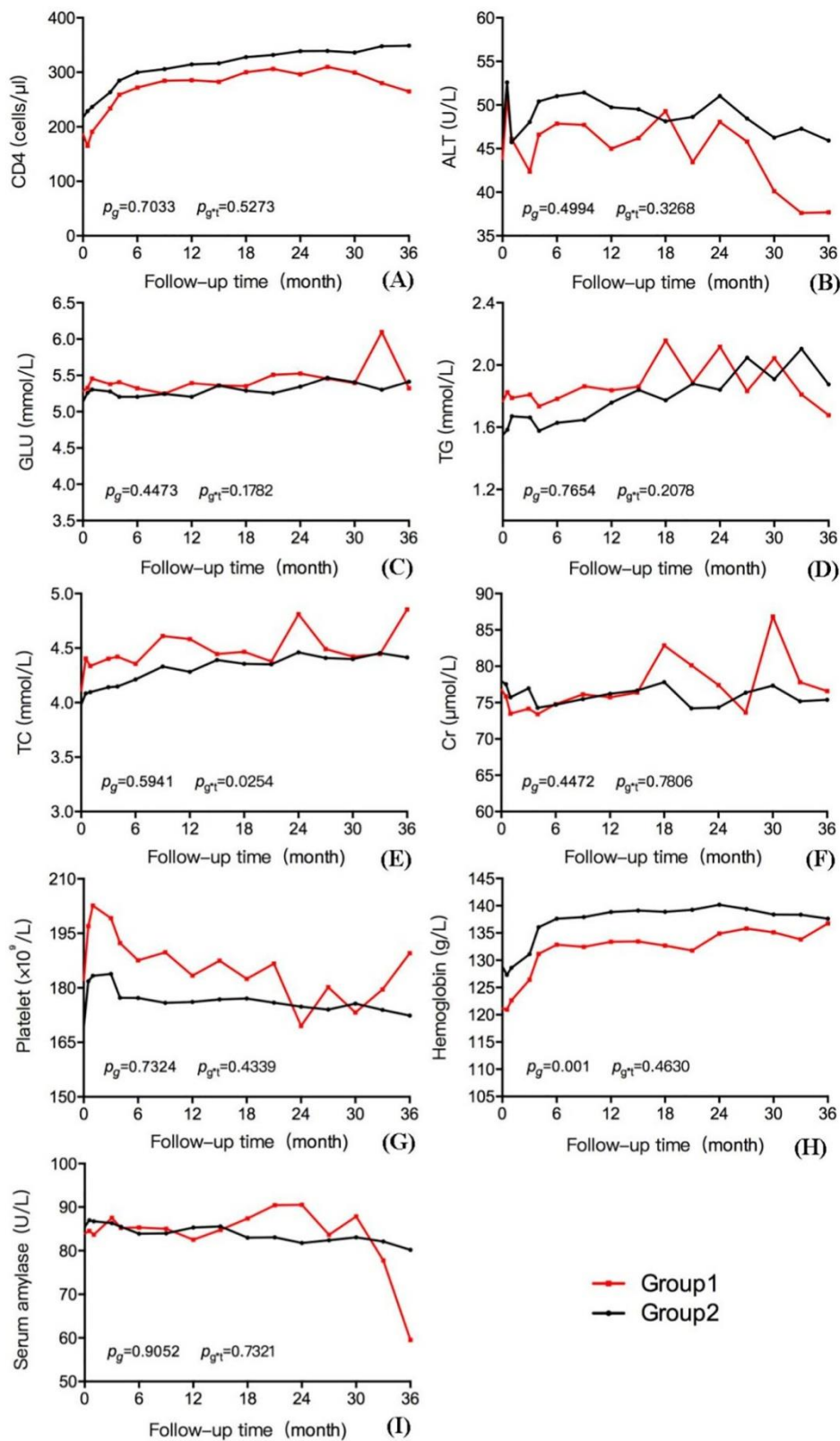


Figure 1: The tendency graph of the primary biochemical indicators

CONCLUSIONS

This study describes the biochemical shifts that occur in HIV-positive individuals both before and after they begin taking antiretroviral medication. The duration of treatment for HIV

patients receiving ART is brief. During the ART process, HIV patients' biochemical indicators (TC and haemoglobin) changed. TC & AST had a substantial effect on the survival time of terminally ill patients, but TG & haemoglobin had a substantial effect on the duration of treatment for patients with drug withdrawal. Variables such as baseline CD4 count, gender, d4T, age & time interval & relationship status can affect patient survival & duration of therapy (single, married). The findings of this study are crucial for the clinical diagnosis and treatment of HIV, as well as for the development of appropriate health measures for HIV patients.

REFERENCES

1. Peters, B.S.; Conway, K. Therapy for HIV: Past, present, and future. *Adv. Dent. Res.* 2011, 23, 23–27.
2. Von Roenn, J.H.; Roth, E.L.; Craig, R. HIV-related cachexia: Potential mechanisms and treatment. *Oncology* 1992, 49, 50–54.
3. Reyskens, K.M.; Fisher, T.L.; Schisler, J.C.; O'Connor, W.G.; Rogers, A.B.; Willis, M.S.; Planesse, C.; Boyer, F.; Rondeau, P.; Bourdon, E.; et al. Cardio-metabolic effects of HIV protease inhibitors (lopinavir/ritonavir). *PLoS ONE* 2013, 8, e73347.
4. Shubber, Z.; Calmy, A.; Andrieux-Meyer, I.; Vitoria, M.; Renaud-Théry, F.; Shaffer, N.; Hargreaves, S.; Mills, E.J.; Ford, N. Adverse events associated with nevirapine and efavirenz-based first-line antiretroviral therapy: A systematic review and meta-analysis. *AIDS* 2013, 27, 1403–1412.
5. Saghayam, S.; Wanke, C. The impact of nutritional status and nutrition supplementation on outcomes along the HIV treatment cascade in the resource-limited setting. *Curr. Opin. HIV AIDS* 2015, 10, 472–476.
6. Estrada, V.; Bernardino, J.I.; Masiá, M.; Iribarren, J.A.; Ortega, A.; Lozano, F.; Miralles, C.; Olalla, J.; Santos, J.; Elías, M.J.; et al. Cardiovascular risk factors and lifetime risk estimation in HIV-infected patients under antiretroviral treatment in Spain. *HIV Clin. Trials* 2015, 16, 57–65.
7. Mendes, E.L.; Andaki, A.C.R.; Amorim, P.R.S.; Natali, A.J.; Brito, C.J.; Paula, S.O. Treinamentofísicopara indivíduos HIV positivos submetidos à HAART: Efeitos sobre parâmetros antropométricos e funcionais. *Rev. Bras. Med. Esporte* 2013, 19, 16–21.
8. Guira, O.; Tiéno, H.; Diendéré, A.E.; Sagna, Y.; Diallo, I.; Yaméogo, B.; Zoungrana, L.; Yaméogo, T.M.; Bognounou, R.; Drabo, J.Y. Features of Metabolic Syndrome and Its Associated Factors during Highly Active Antiretroviral Therapy in Ouagadougou (Burkina Faso). *J. Int. Assoc. Provid. AIDS Care* 2016, 15, 159–163.
9. Zhang, X.; Jiang, X.; Lu, H.; Shen, F.; Wang, J. Dyslipidaemia and Intima-Media Thickness of Carotid Arteries in Thirty-Five HIV/AIDS Patients Receiving Highly Active Antiretroviral Therapy. *Int. J. Biomed. Sci.* 2009, 5, 125–158.
10. Townsend CL, Cortina-Borja M, Peckham CS, Tookey PA. Trends in management and outcome of pregnancies in HIV-infected women in the UK and Ireland, 1990–2006. *BJOG* 2008;115:1078–86.

11. Floridia M, Tamburrini E, Tibaldi C, Anzidei G, Muggiasca ML, Meloni A, et al. Voluntary pregnancy termination among women with HIV in the HAART era (2002–2008): a case series from a national study. Italian Group on Surveillance on Antiretroviral Treatment in Pregnancy. *AIDS Care* 2010;22:50–3.
12. Kaida A, Lima VD, Andia I, Kabakyenga J, Mbabazi P, Emenyonu N, et al. The WHOMEN's Scale (Women's HAART Optimism Monitoring and Evaluation Scale v.1) and the association with fertility intentions and sexual behaviours among HIV-positive women in Uganda. *AIDS Behav* 2009;13:S72–81.
13. Nicopoullos JD, Almeida P, Vourliotis M, GillingSmith C. A decade of the sperm-washing programme: correlation between markers of HIV and seminal parameters. *HIV Med* 2011;12:195–201.
14. Kushnir, V. A., & Lewis, W. (2011). Human immunodeficiency virus/acquired immunodeficiency syndrome and infertility: emerging problems in the era of highly active antiretrovirals. *Fertility and sterility*, 96(3), 546-553.
15. Lazzaretti, R. K., Kuhmmer, R., Sprinz, E., Polanczyk, C. A., & Ribeiro, J. P. (2012). Dietary intervention prevents dyslipidemia associated with highly active antiretroviral therapy in human immunodeficiency virus Type 1–infected individuals: a randomized trial. *Journal of the American College of Cardiology*, 59(11), 979-988.
16. Grulich, A. E., & Vajdic, C. M. (2015, April). The epidemiology of cancers in human immunodeficiency virus infection and after organ transplantation. In *Seminars in oncology* (Vol. 42, No. 2, pp. 247-257). WB Saunders.
17. Pfefferbaum, A., Rosenbloom, M. J., Sassoon, S. A., Kemper, C. A., Deresinski, S., Rohlfing, T., & Sullivan, E. V. (2012). Regional brain structural dysmorphology in human immunodeficiency virus infection: effects of acquired immune deficiency syndrome, alcoholism, and age. *Biological psychiatry*, 72(5), 361-370.
18. da Cunha, J., Maselli, L. M. F., Stern, A. C. B., Spada, C., & Bydlowski, S. P. (2015). Impact of antiretroviral therapy on lipid metabolism of human immunodeficiency virus-infected patients: Old and new drugs. *World journal of virology*, 4(2), 56.
19. Fitting, S., Ignatowska-Jankowska, B. M., Bull, C., Skoff, R. P., Lichtman, A. H., Wise, L. E., ... & Hauser, K. F. (2013). Synaptic dysfunction in the hippocampus accompanies learning and memory deficits in human immunodeficiency virus type-1 Tat transgenic mice. *Biological psychiatry*, 73(5), 443-453.
20. Makinson, A., Pujol, J. L., Le Moing, V., Peyriere, H., & Reynes, J. (2010). Interactions between cytotoxic chemotherapy and antiretroviral treatment in human immunodeficiency virus-infected patients with lung cancer. *Journal of Thoracic Oncology*, 5(4), 562-571.
21. Frantz, J. M., & Murenzi, A. (2013). The physical activity levels among people living with human immunodeficiency virus/acquired immunodeficiency syndrome receiving high active antiretroviral therapy in Rwanda. *SAHARA-J: Journal of Social Aspects of HIV/AIDS*, 10(3-4), 113-118.
22. Menéndez-Arias, L., & Álvarez, M. (2014). Antiretroviral therapy and drug resistance in human immunodeficiency virus type 2 infection. *Antiviral research*, 102, 70-86.