Arch. Bas. App. Med. 2 (2014) 35 - 38

ARCHIVES OF BASIC & APPLIED MEDICINE

Research Article

Fertility Hormones, CD4+T Cells and CD8+Tcells In HIV Seropositive Subjects in Onitsha, Nigeria

Oluboyo, A.O[1], Ihejimkpo, A.E[1]., Onyenekwe, C.C[1]., Oluboyo, B.O[2]., A.O[1] Amah, U.K[1]., Okwara, J.E[1] Ogenyi ,S. I[1]., Onyemelukwe[1]

[1]Department of Medical Laboratory Science, Faculty of Health Sciences and Technology, College of Health Sciences, Nnamdi Azikiwe, University, Nnewi Campus. Anambra State, Nigeria

.[2]PCR Laboratory, Institute of Human Virology, Nnamdi Azikiwe, University Teaching Hospital, Nnewi. Anambra State, Nigeria

Received: May 22, 2013
Accepted: November 25, 2013

Abstract

Human immunodeficiency Virus (HIV) infection and Acquired immunodeficiency syndrome (AIDS) have become global health concern. The uses of antiretroviral therapy (ART) have been shown to improve health but are associated with a wide array of immunologic, endocrinologic and metabolic abnormalities. This study determined the levels of fertility hormones, CD4 and CD8+Tcells in HIV seropositive subjects and seronegative subjects. A total of one hundred and seventy HIV seropositive subjects were investigated while fifty HIV seronegative subjects served as controls. Eighty-five HIV seropositive subjects were on antiretroviral therapy consisting of three drug combinations (Zidovudine 300mg twice daily; Lamivudine 150mg twice daily; Tenofovir 300mg once daily; Efavirenz 600mg once daily and Stavudine 30mg twice daily for body weight of <60kg or 40mg twice daily for body weight of >60kg). Eighty five HIV seropositive subjects were not on antiretroviral therapy. Fertility hormones (Follicle Stimulating Hormone, Leutinising Hormone, Prolactin and Testosterone) were determined using Enzyme linked immunosorbent assay (ELISA) method. CD4+Tcells and CD8+Tcells were determined using flow cytometry. The serum levels of the fertility hormones in HIV seropositive males on antiretroviral therapy (ART) and those not on ART showed significant reduction ($P<0.05$) when compared with that of HIV seronegative male control subjects. The serum levels of the hormones in HIV seropositive females on ART and those not on ART showed no significant difference compared with those of HIV seronegative control female subjects. The CD4+T cell counts of HIV seropositive male and female subjects on ART and those not on ART showed significant reduction ($P<0.05$) when compared with the HIV seronegative control subjects. There was significant increase in the levels of CD8+T cell counts of the HIV seropositive males and females on ART. HIV infection is associated with variations in the male hormonal fertility profiles but without significant effect on women hormonal fertility profiles. However, CD4+Tcells decrease while CD8+T cells increase as HIV/AIDS progresses.

Key words : Fertility hormones, CD4+Tcells, CD8+Tcells, HIV seropositive subjects

INTRODUCTION

Human immunodeficiency Virus (HIV) infection and AIDS have become global health issues of great concern. More than 33 million people around the world are infected with HIV with nearly 5500 dying daily from HIV and AIDS related complications (Myer, 2010). According to Idoko (2013), the current HIV statistic in Nigeria shows that **3.4 million Nigerians are living with HIV and 58.0 % among these are women.** It has been reported that infection by HIV/AIDS and its antiretroviral therapy are associated with a wide array of endocrine and metabolic abnormalities which include adrenal insufficiency, thyroid, hypogonadism and hypopituitarism (Dobs *et al*,1988; Dobs *et al*,1996; Poretsky *et al*, 1995). Although, treatment with antiretroviral drugs increase the life expectancy of people infected with HIV, the virus affects the body's ability to produce and maintain hormone levels. Conde et al,(2009) reported that some drugs that are used to treat HIV related conditions also affect hormone levels. It has also been shown that the HIV infection is associated with altered fertility hormone levels while the antiretroviral therapy may have no effect on the fertility hormones (Ogundahunsi et al,2011). HIV/AIDS also have effects on the immune system. In fact, hypogonadism especially lower testosterone levels have been correlated with weight loss and lower CD4 cell counts (Highleyman, 2010). HIV infects primarily vital cells in the human immune system such as helper T cells (CD4+Tcells), macrophages and dendritics cells (Cunnigham *et al.*, 2010). After initial infection of the human host, the pace of immunodeficiency development, susceptibility to infection and malignancies become manifest and are generally associated with the rate of CD4+ declines (Mandy, 2009). The rate of CD4+ decline varies considerably from person to person and is not constant throughout the stages of HIV infection. CD4 T-cells is the primary but not the only leukocyte that may be infected with HIV (Mandy, 2009). The absolute CD4+Tcell counts provides a powerful laboratory measurement of predicting, staging and monitoring disease progression and response to treatment in HIV- infected individuals (Turner *et al.*,1994;

**Author for correspondence -*
E-mail: adeolaboyo@yahoo.com
Tel: +234-8054168105

Oluboyo et al, 2006) but there are some CD8+Tcells that suppress or regulate the ongoing immune responses (Davenport and Petravic, 2010). These subsets of CD8+Tcells (cytotoxic T-lymphocytes) have the capacity of mediating the lysis of infected autologous cells (Cunningham *et al*, 2010).

Thus, the study set to determine the fertility hormones, CD4+T cells and CD8+T cells in HIV seropositive subjects to see if there are variations in the hormonal fertility profiles in Onitsha, Nigeria.

MATERIALS AND METHODS

The study subjects comprised 170 HIV seropositive adults attending a voluntary counseling and testing (VCT) clinic at Onitsha, Anambra State, Nigeria and 50 seronegative subjects served as control. Eighty-five (85) HIV seropositive subjects were on antiretroviral therapy consisting of three drug combinations (Zidovudine 300mg twice daily; Lamivudine 150mg twice daily; Tenofovir 300mg once daily; Efavirenz 600mg once daily and Stavudine 30mg twice daily for body weight of <60kg or 40mg twice daily for body weight of >60kg) while the remaining eighty five (85) subjects were not on ART. Adequate precautions for collection and handling of blood specimen were observed throughout the research work. The blood specimens for CD4+Tcells and CD8+Tcells were collected into Ethylenediaminetetraaceticacid (EDTA) anticoagulated bottles and were analyzed immediately. The CD4+ and CD8+Tcell counts were determined using Partec cyflow counter (Partec GMBH, Germany). The blood specimens for the fertility hormones were collected into plain specimen containers without anticoagulant. The samples for hormonal assay were allowed to clot and retracted before centrifugation at 1200 rpm for 5minutes using a bench centrifuge. The serum was collected and preserved in a freezer at -20^{o}C until analysis. The hormones were determined using Enzyme immunoassay kits (Diagnostic Automation) and the concentrations of the hormones were determined using Enzyme linked immunoassay (ELISA) reader (STAT Fax – 2100 machine from Awareness Technology, Germany).

Statistical analysis of data

The mean and the standard deviations of the data were obtained using Windows software package for Social Sciences (SPSS) version16. T-test and Analysis of Variance (ANOVA) were used to compare the mean and the standard deviations of the results and P<0.05 was taken as the level of significance

RESULTS

The mean levels of fertility hormones, CD4 + T cells and CD8 +T cells in HIV seropositive subjects and controls are shown in table 1. There were significant decreases in the mean levels of Follicle stimulating hormones (FSH), Leutinising hormone (LH), Prolactin, Testosterone and CD4+ T cells of HIV subjects when compared with the controls. However, there was a significant increase in the mean CD8 +T cells in HIV seropositive subjects compared with the controls. Table 2 shows the mean levels of fertility hormones, CD4 + T cells and CD8 +T cells in HIV seropositive male subjects and male controls. Furthermore, there were significant decreases in the mean levels of Follicle stimulating hormones (FSH), Leutinising hormone (LH), Prolactin, Testosterone and CD4+ T cells of the HIV seropositive male subjects when compared with the male controls.

Table 1 :
Fertility hormones, CD4 + T cells and CD8 +T cells in HIV Subjects on drug therapy, those not on drug therapy and Control subjects

Parameters	HIV Subjects on ART N= 85	HIV Subjects not on ART N= 85	Control N= 50	F-value	p-value
FSH (mIU/ml)	5.40±2.18	5.84± 2.12	6.88±1.45	8.25	0.00*
LH (mIu/ml)	8.68±4.63	8.39±3.55	9.73±2.85	7.20	0.02*
Prolactin (ng/ml)	6.23±2.30	6.53±2.26	7.63±1.99	7.58	0.00*
Testosterone (ng/ml)	2.29±1.70	2.72±0.95	6.17±0.46	8.43	0.00*
CD4 +Tcells (cells /μl)	397.95±186.52	442.96±1223.00	878.86±195.81	79.64	0.00*
CD8 +Tcells (cells /μl)	872.02±242.11	872.76±216.19	440.30±111.17	35.98	0.00*

*Statistically significant at P<0.05

Table 2 :
Fertility Hormones, CD4 + T cells and CD8 +T cells of HIV seropositive and seronegative male subjects.

Parameters	HIV Male Subjects on ART N= 40	HIV Male Subjects Not on ART N= 40	Control Males N= 25	F-value	p-value
FSH (mIU/ml)	5.33±2.25	3.41± 2.01	7.30±1.47	8.868	0.00*
LH (mIu/ml)	6.70±4.35	7.08±3.18	9.95±2.27	7.359	0.00*
Prolactin (ng/ml)	5.45±2.26	6.15±2.26	7.68±2.22	7.672	0.00*
TESTOSTERONE(ng/ml)	4.28±1.70	5.00±1.72	6.17±1.67	9.433	0.00*
CD4 +Tcells (cells /μl)	337.48±127.22	402.55±181.12	937.60±189.67	97.952	0.00*
CD8 +Tcells (cells /μl)	872.02±242.11	916.25±203.37	447.30±120.98	37.540	0.00*

*Statistically significant at P<0.05

Table 3 :
Fertility Hormones, CD4 + T cells and CD8 +T cells of HIV seropositive subjects and seronegative female subjects.

Parameters	HIV Female Subjects on ART N= 45	HIV Female Subjects Not on ART N= 45	Control Females N= 25	F-value	p-value
FSH (mIU/ml)	5.46 ± 2.12	6.21 ±2.23	6.468±1.42	2.458	0.09
LH (mIu/ml)	10.44±4.90	9.69±3.93	9.53±3.43	0.110	0.60
PROLACTIN (ng/ml)	6.93 ± 2.42	6.90 ±2.64	7.57±1.76	0.165	0.48
Testosterone(ng/m)	0.52±0.27	0.43± 0.19	0.46±1.66	0.695	0.490
CD4 +Tcells (cells /µl)	451.71±245.81	478.87±264.88	820.12±201. 94	61.32	0.00*
CD8 +Tcells (cells /µl)	872.02±242.11	834.11±229.00	433.10±101.37	34.41	0.00*

*Statistically significant at P<0.05

There was also a significant increase in the mean CD8 +T cells in HIV seropositive subjects compared with the male controls. Table 3 shows the mean levels of fertility hormones, CD4 + T cells and CD8 +T cells in HIV seropositive female subjects and control females. There were no significant differences in the fertility hormones but there was a significant decrease of CD4+ T cells and a significant increase of CD8+ T cells levels of HIV seropositive female subjects compared with the control females.

DISCUSSION

It has been reported that infection by HIV/AIDS and the use of antiretroviral therapy are associated with a wide array of endocrine and metabolic abnormalities (Highleyman, 2010). There was a significant decrease in the mean serum levels of FSH, LH, prolactin and testosterone in HIV seropositive male subjects when compared with the HIV seronegative control subjects. This finding supports the report of Highleyman (2010). He stated that hypogonadism occurred in a majority of HIV seropositive men. The decrease may be as a result of disturbances in hypothalamic-pituitary-gonadal axis or due to metabolic abnormalities associated with HIV/AIDS. The low testosterone in HIV seropositive patients may results to a variety of symptoms including wasting, fatigue, anaemia, depression and loss of libido which is common to HIV seropositive patients (Highleyman, 2010) especially those with symptomatic HIV diseases.

Furthermore, no significant difference was found in the levels of fertility hormones in HIV seropositive females and HIV seronegative female control subjects. Although, previous studies on the impact of HIV on fertility hormones in women have been inconsistent, our findings are in support of those who suggested that HIV has little or no impact on menstrual function (Shah *et al*,1994; Ellerbrock *et al*,1996). They reported no significant differences in rates of amenorrhea, sparse or heavy menstruation or menstrual cramps between HIV seropositive and seronegative women. However, Ogundahunsi et al (2011) detected a significant decrease in the levels of fertility hormones in HIV women. They reported that treatment with ART improved lives, reduced the risk of opportunistic infections but do not have significant influence on the fertility hormones of HIV infected men and women.

This study also observed a significant decrease in CD4+T cells count and significant increase in the mean levels of CD8+ T cells count in HIV seropositive male and female subjects when compared with the HIV seronegative control subjects. This trend has been shown to be common to all HIV seropositive patients because CD4+Tcells are being attacked by the virus while CD8+Tcells are released to fight the virus (Oluboyo et al,2006; Schelleus *et al.*, 2008). Although, Pohling et al (2010) stated that while antiretroviral suppression of HIV in chronic infection reduces HIV-specific CD8 +T cell response magnitude in the short term, it had no significant effect on response character over periods up to 9 years. However, a recent finding has reported that a subset of CD4+ white blood cells invaded by HIV may control the course of the disease (Cohen, 2013).

We conclude that HIV infection is associated with variations in the male hormonal fertility profiles but without significant effect on women hormonal fertility profiles. However, CD4+Tcells decrease while CD8+T cells increase as HIV/AIDS progresses.

References

Cohen, J (2013): HIV/AIDS : Subset of CD4 Cells May Hold Key to Reaching HIV Cure. *Science* ;339(6125):1262. doi: 10.1126/science.339.6125.1262.

Conde, D.M., Silva,E.T., Amaral,W.N., Finotti,M.F., Ferreira,R.G., Costa-Paiva,L., Pinto-Neto A.M. (2009): HIV reproductive aging and health implications in women. Menopause. 16 (1) 199 -221

Cunningham, A., Donaghy, H., Harman, A., Kim, M., Turville, S. (2010): "Manipulation of dendritic cell function by viruses". Current opinion in microbiology 13 (4): 524–529.

Davenport, M.P. and Petravic, J. (2010): CD8+ T Cell Control of HIV—A Known Unknown. PLoS Pathog 6(1): e1000728. doi:10.1371/journal.ppat.1000728

Délio Marques Conde, Emanuela T. Silva, Waldemar N. Amaral, Marta F. Finotti, Rui G. Ferreira, Lúcia Costa-Paiva, Aarão M. Pinto-Neto (2009) HIV reproductive aging, and health implications in women. Menopause 16 (1) 199 -221

Dobs AS, Dempsey MA, Ladenson PW, Polk BF. (1988) Endocrine disorders in men infected with human immunodeficiency virus. Am J Med. 84:611–616.

Dobs AS, Few III WL, Blackman MR, Harman SM, Hoover DR**,** Graham NM**.** (1996) Serum hormones in men with human immunodeficiency virus-associated wasting. J Clin Endocrinol Metab. 81:4108–4112.

Ellerbrock. T.V., Wright, T.C., Bush, T.J., Dole, P., Brudney, K., Chiasson, M.A. (1996): Characteristics of menstruation in women infected with human immunodeficiency virus. Obstet Gynecol. 87:1030–1034.

Highleyman L. (2010): Inflammation, immune activation, and HIV. Winter-Spring;22(2):12-26

Idoko, J. (2013): Terrifying statistics: 3.4 Million Nigerians Infected with HIV. http://www.informationng.com/2013/11/terrifying-statistics-3-4-million-nigerians-infected-with-hiv.html Assessed on 12/15/2014

Mandy, F.F. (2009): Immunopathology of HIV. In. Cellular diagnostic. Basic principles, methods and clinical applications of flow cytometry. Ulrich, S. Attila, T. Gregor R. (eds) pp. 503 – 507 .

Myer, L., Carter, R.J., Katyal, M., Toro, P., El-Sadr, W.M. (2010): Impact of Antiretroviral Therapy on Incidence of Pregnancy

among HIV-Infected Women in Sub-Saharan Africa: A Cohort Study. PLOS Med 7(2):229.

Ogundahunsi, O. A., Ogundipe, M. O., Akinola, N. O., Soyinka, O. O.Odewabi A. O., Oyegunle, V. A. (2011): The effect of HIV and antiretroviral therapy on fertility hormones in amenorrheic HIV-positive women. African scientist. 2(3):143-146

Oluboyo,A.O.,Okogun,G.R.A.,Duru,L.A.D.Oluboyo,B.O., Emenike E,F.And Obasikene,C.N (2006): Pattern Of Blood Pressure,CD4+ T Cells Count And Some Cardiac Enzymes In HIV Seropositive Subjects. Journal of Biomedical Investigation. 4(2):37-41.

Pohling, J. Zipperlen, K., Hollett, N.A., Gallant, M.E., Grant, M. D. (2010*): Human immunodeficiency virus type I-specific CD8 + T cell subset abnormalities in chronic infection persist through effective antiretroviral therapy.* BMC Infectious Diseases, 10 (129) 1-10.

Poretsky L, Can S, Zumoff B. (1995) Testicular dysfunction in human immunodeficiency virus-infected men. Metabolism. 44:946–953.

Schellens, I.M., Borghans, J.A.M,, Jansen, C.A., De Cuyper, I.M., Geskus, R. B. (2008): Abundance of Early Functional HIV – specific CD8+ Cell Does Not Predict AIDS Free Survival Time. PLOS 3 (7) :2745e. doi: 10.1371/journal.pone.0002745

Shah, P.N., Smith, J.R., Wells, C., Barton, S.E., Kitchen, V.S., Steer, P.J. (1994): Menstrual symptoms in women infected by the human immunodeficiency virus. Obstet Gynecol. 83:397–400.

Turner, B.J., Hecht, F.M., Ismail, R. B., (1994): CD4 + T lymphocytes measures in the treatment of individuals infected with Human Immunodeficiency virus type 1. Arch Intern Med. 194. (154). 1561-1572.