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MONITORING THE VIRAL LOAD IN HIV PATIENTS UNDER ANTI-RETROVIRAL THERAPY (ART)

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Abstract

Viral load monitoring is an important factor in managing HIV disease. Antiretroviral therapy is the recommended treatment for HIV patients, and the goal therapy is achieving viral suppression and reducing viral load below the level of detection. Viral load is an important parameter used to monitor the progression of HIV and critically regarding treatment decision. The results of present study revealed that there were statistical significant differences between patients maintained on treatment (GA) and patients without treatment (GB) regarding the viral load, and clearly indicated that adherence to ART playing a role in suppression the viral load supporting the immune system of HIV infected patients. The success of ART for someone living with HIV depends on, starting the treatment at the right time, choosing the right combination of (ART) and monitoring the effectiveness of the treatment through monitoring the viral load.

Key words: Egypt, HIV patients, ART, viral load.

Introduction

The virus of HIV is transmitted via sexual contact, contaminated blood transfusions, infected needles, prenatal infection from mother to her new born, or during breast-feeding. The virus attacks the immune system causing AIDS disease (Mumtaz *et al*, 2011). Months to years after HIV infection and in the absence of specific treatment as the illness progresses, the virus replicates and can destroy most of the T-cell lymphocytes. This disables the immune system to defend against diseases, tumors and various opportunistic infections will develop.

Viral load should be obtained at diagnosis and may be a factor in deciding when to initiate antiretroviral therapy. Viral load monitoring remains a critical component of HIV care, to evaluate treatment efficacy and provide early warnings of resistance and treatment failure (Keiser *et al*, 2011). Antiretroviral therapy (ART) is the ideal treatment for HIV infection; leads to rapid reduction in HIV RNA plasma levels and increase in peripheral CD4 cell count (Zhou *et al*, 2010; Mocroft *et al*, 2003). Early introduction of ART lead to dramatic reduction in morbidity and mortality associated with HIV infection (Baggaley *et al*, 2008) and decrease the complication as tuberculosis (Abdel Aal *et al*, 2013). WHO (2013) and many national AIDS control programs have adopted guidelines recommending viral load testing 3 to 6 months after initiating ART and then at regular intervals thereafter. ART involves a combination of three or more anti-HIV medications daily, including two nucleoside reverse-transcriptase inhibitors plus non-nucleoside reverse-transcriptase inhibitor or a protease inhibitor (Tebas *et al*, 2013; Bonner *et al*, 2013).

This work aimed to evaluate the efficacy of ART through monitoring the viral load as a tool encouraging treatment adherence in HIV patients.

Patients, Material and Method

This is a prospective study included 260 adult persons who attending to Voluntary Counseling and Testing unite (VCT) in Central Laboratory of Ministry of Health, Cairo, Egypt, in the period from December 2012 to January 2015. All patients had never taken any HIV treatment before. They were divided into two groups; 200 patients started anti-

retroviral therapy against HIV (GA) and 60 patients without treatment (GB), in addition to 30 normal persons considered as controller group (GC). After serum analysis of the HIV patients by multiple ELISA (Gutlapalli *et al*, 2016) and confirmation by western blot techniques, the viral load was measured by quantitative real time PCR (Luchsinger *et al*, 2015) musing QIAGEN, Germany kits & Rotor-Gene Q instrument every 6 months for 24 months.

All patients were clinical and parasitological examined to exclude endemic parasitic disease as visceral leishmaniasis (Mangoud *et al*, 1997), strongyloidiasis, schistosomiasis and filariasis (El-Naggar *et al*, 2006) and cryptosporidiosis (Aboul-Noor *et al*, 2015) due to their wide distribution and potential for severe morbidity and cross-reactivity.

Results

The present study revealed that there were statistical significant differences between patients maintained on ART therapy (GA) and patients without ART (GB) regarding viral load monitoring.

The quantitative real time PCR and its percentage compared to the first reading (base line) were performed to positive HIV patients in both GA & GB (every 6 months for five readings). In GA (patients under ART) was found that the mean of HIV viral load was 52.085, which is highly significant decrease (p<0.0001). There was -96.5% decrease in viral load comparing first reading (base line) to the last one (after 24 months). While in GB (without treatment), the mean of viral load was 3.496 which is highly significant increase (p<0.0083), associated with 612% increase in the viral load comparing first reading to the last one.

This study revealed that 138/200 (69%) patients of GA had viral load more than 10.000 copies/ml. After 24 months of treatment, there was dropping in number of patients having viral load > 10.000 to become 31(15.5%). In GB, 21(35%) patients out of 60 had viral load > 10.000 copies/ml and after 24 months without treatment, number increased to become 32 (53.3%).

In this study, there were 62 (31%) patients in GA with viral load ≤ 10.000) had a significant decrease in viral load earlier than patients who started ART with viral load > 10.000 in the same group. Also, in GA there were 34(17%) patients became PCR negative as there was no virus detected (viral load <20 copies/ml) after 24 months analysis of patients adherent to ART. Details were given in tables (1, 2 & 3) and figure (1).

Table 1: Changes in HIV viral load by real time PCR & % in comparison to 1st reading among **G**A (6 month interval for 24 months of ART)

every 6 months	1st reading	2nd reading	3rd reading	4th reading	5th reading	P -F
Mean± SD	739795± 1168000	246154± 569793	66049± 198812	32239± 120438	31425± 103247	< 0.0001 52.085
Mean % change from 1st reading		-67%	-91%	-96%	-96.5%	%

*p value<0.001(highly significant, *p value>0.05 (non-significant)

Table 2: Changes in HIV viral load by real time PCR & % in comparison to 1st reading among **G**B (6 month interval for 24 months without ART)

every 6 months	1st reading	2nd reading	3rd reading	4th reading	5th reading	P –F
Mean± SD	355551± 1849000	174963± 309619	1623000± 5900000	2701000± 6852000	2531472± 5875423	0.0083 3.496
Mean % change from 1st reading		51%	356%	659.66%	612%	%

Table 3: Changes in viral load in both groups (A & B)

Patients in GA & GB	At start of ART > 10.000 copies / ml	At end of 24 months of ART >10.000 copies / ml
GA (200)	138 (69%)	31(15.5%)
GB (60)	21 (35%)	32 (53.3%)

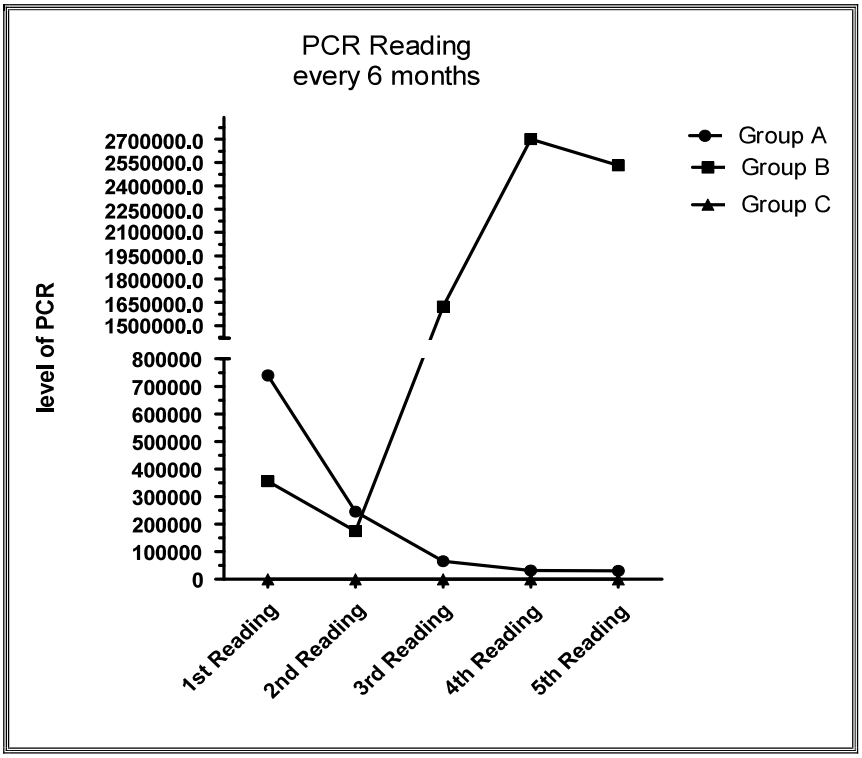

Fig. 1: Different viral load curves among all groups

Discussion

In this study, all patients were parasitic free Lillie *et al.* (2008) in the United Kingdom recommended to screen African HIV patients for schistosomiasis. Costiniuk *et al.* (2012) in Canada recommended screening HIV patients for strongyloidiasis, schistosomiasis and filariasis from parasite-endemic countries to determine factors associated with false-positive serological tests. Faucher *et al*. (2016) in France reported treatment fail in infantile visceral leishmaniasis in concomitant infection with HIV and vice versa. Generally, these parasitic diseases and other were encountered in Egypt (El-Bahnasawy *et al*, 2013; 2014). Wumba *et al.* (2012) recommended epidemiology surveillance, prevention by sensitive PCR and treating opportunistic intestinal parasites that might be acquired via fecal-oral transmission, surface water, normal immunity, rural area-based person-person and animal-human infection and HIV transmission. Therapy, including ART and treatme-nt with specific antiparasitic was a must.

In the present study, regarding the viral load monitoring by quantitative real time PCR in patients under ART (GA), there was highly significant decrease of viral load in proportional to whom did not take ART (GB) through 24 months of analysis. This decreasing rate of viral load in GA reached to undetectable level in most of patients in the first 6 - 9 months of treatment. Regarding patients without treatment (GB), there were significantly high number of viral copies over millions copy/ml.

The present results agreed with Tanser *et al*. (2013) and Saison *et al*. (2013) who revealed low viral load after HAART through two years of treatment. WHO (2010); Vogel *et al*. (2010) and Petoumenos *et al*. (2015) found decreased viral load level or viral suppression in patients' adherent to ART rather than patients without treatment. Tanser *et al*. (2013) found that coverage of ART associated with decline in risk of HIV acquisition in rural South Africa. Also, Hirschhorn *et al*. (2005) in USA reported that initiation of effective antiretroviral therapy

(ART) was probably the most common cause of significant change in viral load seen in clinical practices, with decreasing levels usually occurred within the first weeks of treatment but, in absence of ART, there was increasing viral load levels.

The term viral suppression is used in clinical practice to signify a level of plasma viremia below the level of detection (Tanser *et al*, 2013). In the present study, it was found that (69%) patients from GA having viral load > 10.000 copies/ml. After 24 months of ART, the patients having viral load >10.000 decreased to become (15.5%) patients.

In GB, there were 21(35%) patients having viral load > 10.000 copies/ml and after 24 months of without treatment the numbers increased to become 32 (53.3%) patients. This agreed with Bartlett *et al*. (2005) who found differences among 64 patients under treatment with >10.000 viral load and after follow-up for 24 weeks they became 24 patients >10.000. Also, Hirschhorn *et al*. (2005) found that the number of patients with high level viremia over10.000 copies/ml, decreased after treatment, in contrary to those without treatment. In Wilson *et al*., 2009 study in Thailand reported that, results of 92% patients with persistent low-level viremia achieving viral suppression after additional adherence treatment and counseling. However, Pirkle *et al*. (2009) in Burkina Faso and Mali, found that only one-third of patients received viral-load triggered adherence treatment interventions were able to achieve undetectable viremia.

In this study, about 62 (31%) patients under ART through GA with viral load ≤ 10.000 had a significant decreased in viral load or may reached to undetected viral load earlier than patients who started ART with viral load > 10.000 in the same G after 24 month of ART.

These results were matching with Hughes *et al*. (2011) and Jason *et al*. (2012) where through years of treatment, patients started ART with viral load < 10.000 and CD4 count ≥ 350 had no virologic failure, and there were one or more virologic failure in patients starting ART with viral load above 10,000 copies and CD4 ≤ 350 after 6 - 9 months of treatment. Also, virologic failure with a viral load above 10.000 copies had a greater negative impact on CD4 cell gain than failure with 1000 to 10.000 copies. So, starting of ART in patients having both CD4 ≥ 350 with viral load ≤ 10.000 together had significances to reach undetectable level of viral load and gain more CD4 than others, what is called as virologic success in the first situation, and virologic failure in the second situation (Sterne *et al*, 2009).

In this study, 34 (17%) patients had no detection (viral load <20 copies) through the period of ART in GA, 16 (8%) from them had virological rebound that means detection of the virus in the blood after reach undetected level. Viral loads can jump suddenly in patients under ART treatment for many reasons, including forgetting or irregularity of taking ART, getting another illness such as a sexually transmitted infection, and getting a routine vaccination. Appearance of HIV virus may be associated with changing in CD4 count.

This was in accordance with William *et al*. (2014) that overall 6% of patients had viral load levels below 200 copies after period of undetection of the virus in patients under ART. The phenomenon was more common among those treated during acute or recent HIV infection compared to chro-nically infected individuals. Graham *et al*. (2007) and Konstantopoulos *et al*. (2015) reported that viral load appearance in the blood after a period of no detection. Radjin *et al*. (2008) found that viral rebound was associated with declined CD4 count. Li *et al*. (2014) found detectable levels of viremia accompanied with higher CD4 count after vaccination of patients under ART. They added that vaccine-induced T-cell re-sponse was associated with a modest transient effect on residual viremia, but more potent immune responses and/or combination treatment with the latency-reversing agents are needed to reduce the

HIV reservoir. HIV reservoir measures may act as biomarkers of post-ATI viral rebound kinetics.

Conclusion

Switching patients with persistently undetectable HIV-1 viremia under antiretroviral treatment (ART) to treatment is a cost-effective and well-tolerated strategy. Thus, proper diagnosis is a must. There is a necessity for implementation of improved and economically systematic attempt that allows clinicians to make a rational choice of therapy regimen to overcome the first-line therapy failures among ART-naive.

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