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Original article

Comparative cross-sectional study of interferon γ inducible protein- 10 in mono and co-infected human immunodeficiency virus patients in Alexandria, Egypt

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ABSTRACT

Background: Human immunodeficiency virus (HIV) infection is a global health issue. Upon invasion, the virus induces many inflammatory cytokines; especially interferon- γ induced protein 10 (IP-10). The aim of our study was to detect and compare the serum IP- 10 levels in HIV mono- infected, hepatitis C virus (HCV) mono- infected patients, and HIV co-infected patients with HCV. **Methods:** The study included 30 HIV patients (15 mono- infected and 15 co-infected with HCV), 15 HCV infected patients and 15 healthy controls. HIV RNA, HCV RNA, CD4+T cell counts, IP-10 levels and Fibrous -4 score were estimated. **Results:** The mean value for HIV PCR was $1.04 \times 10^4 \pm 3.86 \times 10^4$ in HIV co-infected patients and $4.14 \times 10^7 \pm 1.58 \times 10^8$ in HIV mono-infected patients. The highest mean value for FIB-4 scores and CD4+T cell counts were among HIV co-infected patients; 1.56 ± 2.17 and 432.80 ± 294.83 respectively. HCV mono-infected patients revealed the highest IP-10 mean value; 472.0 ± 235.28 . No significant difference was found in HIV co-infected ($p=0.806, 0.327$) nor HIV mono-infected patients ($p=0.244, 0.581$) regarding the relation between CD4+T counts (> 400 or < 400) with the IP-10 levels and FIB-4 scores respectively. **Conclusions:** High IP-10 levels were associated with low CD4 cell count in HIV mono and co-infected patients. IP-10 secretion may be related to HIV pathogenesis and immune depletion. HIV/HCV co-infection did not influence HIV disease progression.

Introduction

Human immunodeficiency virus (HIV) infection is a crucial health issue [1]. In 2021, approximately of 29,000 of adults aged 15 years and

above are living with HIV in Egypt [2]. Early detection is important to reduce the occurrence of life-threatening HIV- related malignancies, cardiovascular, pulmonary, gastrointestinal

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complications and opportunistic infections as *Candidiasis*, *Cryptococcosis*, *Cryptosporidiosis*, *Tuberculosis*, *Toxoplasmosis*, *Cytomegalovirus* infections [3]

Upon invasion and replication of HIV, the expression of several inflammatory cytokines is induced. Interferon- γ (IFN- γ) induced protein 10 (IP-10) is main cytokine involved [1]. IP-10 (also known as CXCL 10) is a chemokine that is produced in response to interferon -gamma. IFN- γ [4]. It is secreted from monocytes, lymphocytes, endothelial cells, stromal cells and keratinocytes [5]. Endogenous cytokines and exogenous lipopolysaccharides may also stimulate the secretion of IP-10 [6].

IP-10 levels are rapidly escalated after HIV infection. This chemokine stimulates viral replication, thereby increasing viraemia [7]. The increased production of IP-10 during HIV -1 infection was conferred to HIV-1 accessory protein Trans activator of transcription (Tat), present in astrocytes and macrophages [8]. The pivotal role of IP-10 is the attraction and recruitment of lymphocytes to their inflammatory binding receptors, CXCR 3. It specifically attracts T cells, NK cells and monocytes, suggesting its role in the development of inflammation [6]. In the course of HIV infection, IP-10 levels are greatly correlated with viral loads and CD4+T cell counts even in untreated primary HIV infected patients [7]. IP-10 levels decline after the initiation of Highly Active Antiretroviral Therapy (HAART) in acute and chronic HIV-infected patients [9] and its use as a prognostic marker of treatment outcome [6]. IP-10 also facilitates the replication of HCV and is used as a pretreatment baseline biomarker for determining treatment options for these patients [10]. Previous studies have reported the increase of IP-10 levels in both HIV mono and co-infected patients with HCV [5, 6, 11-13].

Our study aimed to detect and compare the serum IP- 10 levels in HIV mono- infected, HCV mono- infected patients, and HIV co-infected patients with HCV.

Methods

Study design

This cross- sectional study included 45 patients that were subdivided into 3 groups. Group I included 15 HIV/HCV co-infected patients, group II comprised 15 HCV infected patients, group III included 15 HIV mono-infected patients. In addition 15 healthy

individuals (serologically tested to be free from HIV, HCV and HBV infections) represented the control group IV.

All participants were recruited from the outpatient clinic of the Alexandria Hepatology, Gastroenterology and Infectious Disease Hospital, Alexandria, Egypt. Samples were collected during a six months period in the year 2018. All participants freely volunteered in the study and informed consents were taken. Ethical clearance was attained from the Ethics Committee, Institutional Review Board of the Medical Research Institute [IORG# 0008812]. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

The aim of the study was clarified to each participant before enrollment. Privacy and confidentiality were ensured to all participants throughout the research study. Inclusion criteria comprised patients that were HIV positive, HCV positive or both; and the minimum age was above 18 years. HIVmono -infected and co-infected patients were on HAART for at least one year. HCV mono-infected and co- infected have not received anti-HCVtherapy. Exclusion criteria included being serologically negative for Hepatitis B virus infection and an age below 18 years. The diagnostic criteria for HIV infection was the detection of specific antibodies[14]. HCV infection was diagnosed by the detection of reactive antibodies and HCV RNA [15]. A 10 ml. of blood was drawn from each patient to be used in the following tests.

Liver enzymes

Alanine transaminase (ALT), aspartate transaminase (AST) and platelet counts were estimated for all patient groups and controls.

Virology profile

HIV laboratory tests

HIV antibodies detection were performed using Enzyme linked Immunosorbent assay(Human anti-HIV 1+2 ELISA Kit, IVDEIA002, London, UK) and confirmed using the Western blotting technique (Cambridge Biotech Co., Rockville, Maryland, US.) They were conducted according to the manufacturer's instructions. HIV RNA-PCR viral loads were obtained from the clinical data records for each patient.

HCV laboratory tests

Hepatitis C virus antibodies detection were carried out, conferring to the manufacturer's instructions using third generation HCV ELISA kit (Z01370,

Dialab, Austria). Quantitative detection of HCV RNA HCV was performed using Real Time PCR. RNA extraction was conducted using Qiagen QIAamp viral RNA mini spin protocol. (No. 52904). The extracted 10µl of RNA was amplified using HCV Qiagen kit (Artus, QS-RGQ (72) ref.4518366 HCVPCR kit) RNA protocol using TaqMan technique. The Real Time -PCR reactions were assayed in a final volume of 25 µl using the PCR MX3000 Strategene system(Applied Biosystems Inc., California,U.S). The reaction was conducted under the following thermal profile: Incubation at 50 °C for 30 min (reverse transcriptase step), followed by AmpliTaq gold activation for 95° C for 10 min., then 40 cycles of two step amplification, denaturation for 95° C for 15 sec. This was followed by annealing at 60° C for 1 min., and extension at 72° C for 30 min. Melting curve analysis was performed after final amplification by heating samples at 95° C for 60 sec, cooling to 55° C for 30 sec., and heating to 95° C for 30 sec with continuous fluorescence recording. Melting curves were recorded and PCR products were investigated using 2.5% agarose gel electrophoresis.

CD4+T estimation by flow cytometry

It was performed using CD4+T easy count kit (Code no. 05-8401, Partec, Germany). A 20 µl whole blood (anti- coagulated with EDTA) was added to a Partec test tube. Then 20 µl of CD4+T mAb PE (MEM – 241, PE- conjugated mAb to human CD4+T was added, gently mixed and incubated for 15 min. at room temperature away from light. A 800 ul of no lyse buffer was added and gently shaken. The blood sample was analyzed on a Partec device. The absolute concentration of CD4+T cell was displayed as the number of cells / ul whole blood.

Evaluation of IP-10 levels (pg/mL)

IP- 10 levels were determined using Human IP-10 instant high sensitivity ELISA (BMS284INST, e Bioscience, U.S). The procedure was conducted according to the manufacturer's protocol instructions. Absorbance was read for each microwell using a spectrophotometer of 450 nm as the primary wavelength. Reference wavelength ranged from 610 nm to 650nm. The absorbance of the samples and IP-10 standards were measured in picograms per milliliter (pg/mL). The standard curve range was 8.23-6000 pg/mL with a sensitivity of 8 pg/mL.

Liver fibrous score

It was calculated for all patient groups and controls using the following formula:

$$\text{Fib-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}$$

Statistical analysis

Data was analyzed using IBM SPSS software package version 20.0 (Armonk, NY: IBM Corp). Qualitative data were designated by number and percent. Shapiro-Wilk test was used to verify the normal distribution. Quantitative data were described using minimum and maximum ranges, mean, standard deviation and median. Significance of results were arbitrated at the 5% level. Chi-square test, Fisher's Exact or Monte Carlo correction, Mann Whitney test, Kruskal Wallis test and Spearman coefficient were also used.

Results

Demographic data

The study included 45 patients from which 29 (64.5%) were males and 16 (35.5%) were females. Group I included 12 (80%) males and 3(20%) females. Group II comprised 4 (26.7%) males and 11(73.3%) females. Group III included 13(86.7%) males and 2 (13.3%). Group IV (controls) comprised 6 (40%) males and 9 (60%) females. The mean ages ranged from 37.53 ± 5.45 for group I patients; 53.87 ± 10.13 for group II patients, and 36.20 ± 12.51 for group III patients; while the mean age for the controls was 35.47 ± 13.10 .

Liver enzymes

AST levels (U/L)

Table 1 displayed a significant difference was found between groups I and III ($p = 0.011$), and also between groups II and III ($p = .024$).

ALT levels (U/L)

Table 1 showed a significant difference was also found between groups I and III ($p = 0.011$), and also between groups II and III ($p = 0.006$).

Platelet count (per µL of blood)

The highest count was represented by the control group IV, where the mean value was (253.3 ± 056.17). This was followed by group I where the mean platelet count was (230.67 ± 106.92), group II (214.80 ± 47.92) and the lowest count was recorded in group III (204.0 ± 45.16).

A significant difference was found between the four groups ($p = 0.044$).

Virology profile

The mean value for HIV PCR was $(1.04 \times 10^4 \pm 3.86 \times 10^4)$ in HIV co-infected Group I patients and was $(4.14 \times 10^7 \pm 1.58 \times 10^8)$ in HIV mono-infected group III patients. No statistical significance was found between both groups ($p=0.063$). Regarding HCV PCR, the mean values in group I patients was $(3.06 \times 10^6 \pm 2.79 \times 10^6)$, while the level in group II patients was $(4.95 \times 10^6 \pm 5.31 \times 10^6)$. Again, no statistical significance was found between these two groups ($p=0.290$).

CD4⁺T estimation (cells/mm³)

It was conducted in groups I and III, where the number of patients who recorded a CD4⁺T < 400 in each group was 10 (66.7%) and > 400 was 5 (33.3%). Results were not found significant between both groups ($p=1.000$). Moreover, the CD4⁺T count was relatively higher in group I compared to group III (Table 2). No significant difference was found between both results ($p=0.455$). A negative correlation between CD4⁺T, HCV RNA and HIV RNA levels in group I, HIV co-infected patients ($r = -0.454, p = 0.089$ / $r = -0.265, p = 0.339$) was respectively revealed. On the contrary, a positive correlation between CD4⁺T and HIV RNA levels in Group III, HIV patients was found ($r = 0.015, p = 0.959$).

Evaluation of IP-10 levels

Table 1. Comparison of liver enzymes between patients and control groups.

Liver Enzymes (U/L)	Patients (n=45)			Group IV Control (n=15)	H	p
	Group I HIV /HCV (n=15)	Group II HCV (n=15)	Group III HIV (n=15)			
AST						
Min. – Max.	10.50 – 203.0	18.0-70.0	9.0-37.0	4.0 – 14.0	38.159*	<0.001*
Mean ± SD.	50.30 ± 45.67	38.07 ± 16.56	21.92 ± 8.45	8.60 ± 3.04		
Median	40.0	35.0	22.0	9.0		
<i>p</i> 1	<0.001*	<0.001*	0.004*			
Sig. bet. Gps.	$p_2=0.778, p_3=0.001^*, p_4=0.024^*$					
ALT						
Min. – Max.	8.0 – 145.0	20.0-96.0	9.0-57.0	5.0 – 16.0	36.669*	<0.001*
Mean ± SD.	57.0 ± 40.05	46.27 ± 20.57	21.94 ± 11.79	9.67 ± 3.35		
Median	47.0	40.0	20.0	10.0		
<i>p</i> 1	<0.001*	<0.001*	0.013*			
Sig. bet. Gps.	$p_2=0.842^*, p_3=0.011^* p_4=0.006^*$					

H and p values for **Kruskal Wallis test** Pairwise comparison between each 2 groups (Post Hoc Test; Dunn's multiple comparison test)

p= probability value

*p*1=*p* value for comparing **Group IV** and other groups

*p*2=*p* value for comparing **Group I** and **Group II**

*p*3=*p* value for comparing **Group I** and **Group III**

*p*4=*p* value for comparing **Group II** and **Group III**

*Statistically significant at $p \leq 0.05$

Table 3 showed that the highest level for IP-10 was among the HCV patients (Group II).

A significant difference was found in the IP-10 levels between the three patient groups ($p=0.008$). Moreover, a significant difference was also found between group II and the control group IV ($p=0.001$).

Liver fibrous score

Table 4 showed that group I revealed the highest FIB-4 score, followed by groups II, then III; while the lowest score was recorded in the control group. A significant difference was found between patients and control groups ($p=0.001^*$) and also between groups II and III ($p=0.026^*$).

On the other hand, no significant correlation was found between IP-10 levels with AST ($r = 0.199, p = 0.189$), ALT ($r = 0.243, p = 0.107$), platelet counts ($r = -0.261, p = 0.083$), HIV RNA ($r = 0.061, p = 0.747$), HCV RNA ($r = -0.138, p = 0.467$) and CD4⁺T counts ($r = -0.180, p = 0.342$) in all three patient groups.

Regarding the relation between CD4⁺T counts (> 400 or < 400) in groups I and III with the IP-10 levels and FIB-4 score; no significant difference was found in either of group I ($p = 0.806, 0.327$) or group III ($p = 0.244, 0.581$) respectively. However a significant positive correlation was revealed between IP-10 levels and FIB-4 score in all patient groups ($r = 0.006^*, p = 0.006^*$).

Table 2. Comparison of the CD⁴ T cell counts between patient groups I and III.

CD ⁴ T cell counts cells/mm ³	Group I HIV /HCV (n=15)	Group III HIV (n=15)	U	p
Min. – Max. Mean ± SD. Median	83.0 – 936.0 432.80 ± 294.83 295.0	83.0 – 868.0 359.27 ± 240.79 267.0	94.50	0.455

U and p values for **Mann Whitney Test** for comparing between the two groups
p= probability value

Table 3. Comparison of the IP-10 Levels between patients and control groups.

IP-10 level. (pg/ml)	Patients (n=45)			Group IV Controls (n=15)	H	p
	Group I HIV /HCV (n=15)	Group II HCV (n=15)	Group III HIV (n=15)			
Min. – Max. Mean ± SD. Median	80.0-1540.0 361.0±411.39 240.0	140.0-890.0 472.0±235.28 410.0	100.0-1500.0 316.0±352.32 200.0	60.0-570.0 212.0±144.38 170.0	11.730*	0.008*
p1	0.233	0.001*	0.377			
Sig. bet. Gps	p 2 =0.035*, p 3= 0.758, p 4=0.016*					

H and p values for **Kruskal Wallis test** Pairwise comparison between each 2 groups (Post Hoc Test; Dunn's multiple comparison test)
p= probability value

p1=p value for comparing **Group IV** and other groups

p2= p value for comparing **Group I** and **Group II**

p3= p value for comparing **Group I** and **Group III**

p4= p value for comparing **Group II** and **Group III**

*Statistically significant at $p \leq 0.05$

Table 4. Comparison of the fibrous score between patients and control groups.

FIB - 4	Patients (n=45)			Control (n=15)	H	p
	Group I HIV /HCV (n=15)	Group II HCV (n=15)	Group III HIV (n=15)			
Min. – Max. Mean ± SD. Median	0.56 – 9.28 1.56 ± 2.17 0.92	0.38-2.85 1.54±0.74 1.37	0.32-2.23 0.87±0.46 0.77	0.19 – 0.69 0.40 ± 0.16 0.44	32.794*	<0.001*
p1	<0.001*	<0.001*	<0.001*			
Sig. bet. Gps	p 2 =0.259, p 3= 0.272, p 4=0.026*					

H and p values for **Kruskal Wallis test** Pairwise comparison between each 2 groups (Post Hoc Test; Dunn's multiple comparison test)

p= probability value

p1=p value for comparing **Group IV** and other groups

p2= p value for comparing **Group I** and **Group II**

p3= p value for comparing **Group I** and **Group III**

p4= p value for comparing **Group II** and **Group III**

*Statistically significant at $p \leq 0.05$

Discussion

Hepatitis C virus-HIV co-infected patients exhibit rapid progression of liver damage relative to HCV mono-infected patients [16]. In our work, liver function tests were highest in Group I co-infected patients compared to both mono-infected groups. Our data agreed with other studies that postulated that HIV enhances and accelerates the course of HCV-related liver disease [16,17].

Human immunodeficiency virus may also lead to hepatic disease by activating hepatic stellate cells, stimulating collagen and pre-inflammatory cytokines [18]. It may accelerate the progression of HCV hepatic disease, doubling the risk of cirrhosis. HIV has been associated with hepatic fibrosis even in the absence of viral hepatitis [19].

The mechanism of hepatic disease in HCV, HIV, and HIV co-infected patients is diverse. It includes oxidative stress, and an immune response with generalized inflammation [20]. The pathophysiology of hepatic fibrosis is multifactorial in HIV infected patients; namely persistent viral replication and bacterial translocation leading to chronic immune activation and inflammation. This in turn will promote the release of fibrinogen mediators resulting in fibrosis [19].

In our study the highest FIB-4 score was found in the HIV/HCV co infected patient group. A slightly lower score was found in the HCV infected patients and the lowest score was among HIV mono-infected patients. No fibrosis was found in the control group. Patients with a low score are not required to undergo a liver biopsy, however those with high scores may require a biopsy to confirm hepatic disease. Liver biopsies were not performed for our patients as their FIB-4 scores indicated that they did not have liver fibrosis. The relatively high FIB-4 score in HCV patients may be attributed to not receiving anti-HCV treatment [21].

Human immunodeficiency virus /HCV co-infection may lead to accelerated hepatic fibrosis progression, higher rates of liver failure, and death compared to patients with HCV mono -infection. This acceleration can be hindered with successful control of HIV with HAART [22]. Patients with HIV/HCV coinfection develop hepatocellular carcinoma at younger ages, with more symptoms than those with HCV mono -infection, suggesting a synergy between both viruses, resulting in oncogenesis [23].

Liver biopsy is the gold standard for the clinical diagnosis of hepatic fibrosis; however, its invasive nature may contraindicate its use in HIV patients. Laboratory diagnosis using FIB-4 score is a non-invasive test that could be used to assess the progression of liver disease with a good predictive accuracy. The FIB-4 score evaluates the degree of fibrosis in patients suspected or already diagnosed with hepatic fibrosis [21].

Cytokines and chemokines play a significant role in the pathogenesis of HIV infection [1].

T cells produce large amounts of IP-10 during active HIV infection, which in turn attract a large number of susceptible T cells to the lymph nodes. These T cells become stranded and retained in the infection lymph nodes. This may enable the spread of the virus and potentially facilitate the progression of HIV infection [24].

IP-10 is produced by hepatocytes, where its transcription and the expression of the IP-10 receptor CXCR3 on lymphocytes infiltrating the liver are increased in patients with chronic HCV infection indicating the role of IP-10 in the pathogenesis of HCV-induced liver damage [25]. The role of IP-10 in HIV/HCV co-infection is not completely clear. However, there is evidence that it is associated with other biomarkers of HIV or HCV infections and may be regarded as a predictive biomarker for severe viral replication in these patients [26].

In the present study all HIV infected patients received HAART for a duration of 12 to 18 months, providing a manageable control for disease progression. The highest IP-10 level was found in HCV Group II infected patients. This may be attributed to that all HCV mono-infected patients did not receive treatment for HCV. Moreover, IP-10 levels were significantly different between the 3 patient groups and the healthy controls. Lower IP-10 levels in both HIV mono and co-infected could be explained by the fact that these patients had received HAART. IP-10 levels were higher in HIV co-infected patients compared to the mono-infected patients. This finding was also reported by **Roe et al.** in which IP-10 levels were positively correlated with the degree of liver fibrosis and the level liver enzymes in co-infected patients [12]. However no substantial difference was found in IP-10 levels between both patient groups in our study. HAART suppresses and controls HIV replication, maintains

the function of the immune system, by resorting the numbers of CD4 T-cells, reduces inflammation and prevents opportunistic infections which often lead to mortality [27].

Highly active antiretroviral therapy decreases IP-10 levels [28]. IP-10 levels were found to decrease significantly within 2 years after initiation of therapy. Throughout HAART, the production of IP-10 is decreased in most of HIV infected patients; however, their levels continue to be higher compared to uninfected individuals [16]. **Valverde-Villegas et al.** reported that patients who had undergone two years of HAART have effectively reduced IP-10 levels compared to those who received treatment for only one year [13].

Chronic immune activation in HIV infection is associated with accelerated HIV disease progression [29]. Highly active antiretroviral therapy lowers immune activation, but does not eliminate it, despite an effective decrease in viral load [13]. In chronic HIV infection, the sustained production of IFN- γ is accountable for the persistent increase in IP-10 levels [30].

Previous studies reported that peripheral and intrahepatic increase in IP-10 levels is related to more liver damage [6, 28,29]. Our study revealed similar findings, where the high levels of IP-10 in HCV-mono-infected patients were associated with an increase in HCV RNA, ALT, AST and FIB-4. Since these findings are correlated with an increase in liver disease, this may partially explain the cause of slight advancement to liver disease in HIV/HCV co-infected patients.

Plasma IP-10 levels are strongly associated with CD4+ T cell counts and viral loads during HIV infection [16, 28,30]. In our study the CD4+T cell counts were higher in the HIV co-infected compared to HIV mono-infected patients. The relation between IP-10 levels and CD4+T cell counts (below and above 400) was found to be inversely proportionate. IP-10 levels were found to be higher in the patients with CD4+T cell counts < 400 compared to those with CD4+T cell counts > 400. Similar findings were reported in several previous studies where, IP-10 levels positively and negatively correlated to viral loads and CD4+T cell counts, respectively. Pre-infection systemic the levels of IP-10 prior to HIV infection are closely related to the loss CD4+T cells post-infection [31]. Post-infection IP-10 levels are also inversely correlated to CD4+T cell counts, whether the patients have undergone therapy or not [7,32].

Weak HCV-specific memory CD4 T cells in HIV may contribute to lower rates of HCV clearance. Moreover, a decrease in HCV-specific IFN-gamma secreting CD4 responses in HIV/HCV-coinfected patients may occur, independent of CD4 cell count [33].

This may be explained by the immune activation that takes place during HIV infection that may contribute to CD4+T cell depletion. In addition, the incomplete recovery of the adaptive immune responses may result in a decrease in CD4 T-cell proliferation among HAART-treated adults [34].

A maintained CD4+T cell response is mandatory for prolonged HCV/RNA suppression and protection from secondary infection. On the other hand, the loss of CD4+T cell reactivity in the acute phase of infection is accompanied with the re-occurrence of HCV/ RNA [35]. Patients with higher HCV/ RNA potentially cause a strong negative impact on the development of an effective immune response, which in turn may further facilitate HCV replication [36].

Persistent elevation of IP-10 levels throughout HAART in patients; despite suppressed viral levels are distinguished as responders and non-responders. Responders reveal a sharp reduction in IP-10 levels after HAART. On the other hand, non-responders may show increased IP-10 levels; thereby denoting that IP-10 is useful for distinguishing between responders and non-responders [37]. All HIV mono-infected patients were responders to ART in our study; with a mean of HIV RNA less than 20 copies.

The lack of an association between HIV/HCV co-infection and HIV disease progression remains controversial [38]. The threat of immunological depletion may increase with the persistence of immune activation in spite of the decline in the viral load. Hence monitoring of immune activation is important in the management and control of mono and co- infected HIV patients [39].

Conclusions

High IP-10 levels were associated with low CD4 cell count in HIV mono and co-infected patients. Thus, the pathogenesis and immune depletion in HIV infected patients could be related to IP-10 secretion. HIV/HCV co-infection did not influence HIV disease progression. No significant correlation was found between IP-10 levels and liver enzymes, platelets, viral load and CD4+T cells.

Limitations

There were several limitations to our analysis. Liver biopsy was not performed in these patients because such an invasive procedure may increase the risk of infection and rarely change the clinical management. Our work focused on the current HAART taken at the time of the study and did not take into account past HIV therapy. Patients may change their HAART regimen because of drug toxicities, compliance issues or development of drug resistance. Unfortunately, the number of participants enrolled in this study were limited in number due to the social and religious considerations, rendering it difficult to openly claim and disclose their disease.

Declaration of interest

The authors report no conflicts of interest.

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Author's Contribution

Abeer A. Ghazzal, and Ibtisam F. EL Ghazawy contributed to the conception and design of the study. Fatma T. Mohammed collected the clinical data and samples from the patients. Dalia EL Sayed Metwally and Fatma T. Mohammed conducted the laboratory work. Gihan Adel ELbatouti and Abeer A. Ghazzal conducted the analysis and interpretation of the data. Gihan Adel ELbatouti contributed in writing, drafting of the paper for publication. All authors revised the paper critically for intellectual content. All authors approved the final version to be published. All authors agree to be accountable for all aspects of the work.

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