Comparison of Adenosine Deaminase, Zinc, Magnesium, Lipid Profile, and some Micronutrient Elements and their Relation with CD4 Counts in Human Immunodeficiency Virus Positive and Negative Patients

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ABSTRACT

Background: There is strong evidence regarding the patterns of alteration in the blood parameters in human immunodeficiency virus (HIV)-positive patients. However, no consensus has been reached in this regard and the results vary from different regions and studies. Our study aims to report these patterns in a population of HIV-infected patients in Iran. **Materials and Methods:** We studied two groups of HIV-infected and HIV-negative patients. One hundred and fourteen subjects were enrolled in each group; blood parameters were compared in these two. **Results:** Variables of HIV-negative patients changed as follows compared to HIV-positive patients: with regard to the hematological variables, CD4+↓; CD8+↓; WBC↓; RBC↓; HCT↓; MCV↑; MCH↑; MCHC↑; PLT↓; EOS↑; and BASO↑; and among the metabloic parameters, TG↓; CH↑; HDL↓; LDL↓, MG↑; ZN↑; P↑; and ADA↓, which showed significnat differences between groups ($P < 0.05$). **Conclusion:** We conclude that HIV infection affects hematopoiesis by diminishing the hematological productivity parameters and increasing red blood cell related morphology, along with a different pattern of lipid profile (decreased TG, LDL, HDL, and increased CH) and serum micronutrients (elevated concentration of serum trace elements) in our population of study.

Key words: Adenosine deaminase, HIV, Magnesium, Zinc

INTRODUCTION

Given the ongoing incidence of human immunodeficiency virus (HIV) infection,[1] thanks to the effectiveness of antiretroviral therapy (ART), especially its well-known subclass of protease inhibitors (PIs)[2] that are coming up every day, HIV-infected patients are going to live longer than ever before.[1] In addition to the special healthcare that is essential in this population at an older age, metabolic alterations and organ function deterioration may neccesitate another concern in this regard. With the advent of the highly active antiretroviral therapy (HAART),[2] the history of HIV-related complications has been splitted in terms of hematological parameters and biochemistry, as these parameters have been shown to be affected in relation to the long-term administration of this class of drugs.[3-6] In addition, hematological alterations, including diminished white blood cells, thrombocytopenia, and decreased red blood cells (anemia) have been already reported in patients diagnosed with the acquired immunodeficiency syndrome (AIDS) regardless of the antiretroviral therapy.[5,6] This is besides the abnormal pattern of lipid profile already demonstrated in HIV-infected subjects.[3-4,7] Bone marrow failure occurs apparently in association with type-1 HIV infection and by impacting on hematopoiesis, cytopenia is commonly seen in this population.[6,8,9]

With the increasing number of HIV-infected patients who have access to HAART,[1] it seems that blood evolutions raise more issues each day. Hence, it is of absolute importance to pay attention to this subject not only due to the alteration of parameters, but for the sake of its impacts on HIV-related mortality and progression of the viral infection to the more advanced stages of the disease.

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Although there are a large number of studies around the subject of hematological alterations in patients with HIV infection, such reports does not exist in Iran. Also, it seems that different studies with their small size have only assessed one aspect of these evolutions and not all the hematological changes have been brought into the circle.[10] Besides, the increasing incidences of HIV infections that are occurring in our population necessitate more attention in this regard, before such issues become prevalent in the country just like they did, some years ago, in the rest of the world.

The aim of our case-control study was to determine the hematological alterations, lipid profile patterns, and some of the other biochemical elements (micronutrients) in the HIV-infected population, by referring to an academic referral hospital in Tehran, the capital of Iran.

MATERIALS AND METHODS

Our case-control study was carried out prospectively at Imam Complex, a major referral hospital in Tehran, the capital of Iran, affiliated to the Tehran University of Medical Sciences (TUMS). A group of 114 patients already diagnosed as HIV-positive cases referring to the center of high-risk behaviors from January 2011 to June 2011 were included in the study. The diagnosis was made based on western blotting, the enzyme-linked immunosorbent assay (ELISA), and the polymerase chain reaction (PCR). The control group comprised of 114 cases with negative results for complete HIV testing performed at the Imam Complex in TUMS, Tehran, Iran. Age and other demographics were matched and the confounding factors were all adjusted.

Patients with a history of serious medical diseases including autoimmune disease, corticosteroid administration, previous diagnosis of viral infections, malignancy, pregnancy, gastrointestinal tract (GI) disorders, including malabsorption, children (age < 18 years old), patients who were receiving antibiotics in the prior two weeks, and patients who could not to be evaluated by western blot were excluded from the study.

Five milliliters of clotted blood and 3 ml of anticoagulated blood by ethylenediaminetetraacetic acid (EDTA) were obtained by needle aspiration from a circumferentially and superficially sterilized vein, and were sent to the laboratory of the hospital later. The clotted blood was centrifuged by 3,000 g for 15 minutes. Serums were extracted before being stored in a -70ºC freezer for further evaluation. As the collection of serum samples reached the desired number, the hematological parameters, lipid profiles, and biochemical elements were measured at room temperature for each patient.

Anticoagulated blood was also tested in terms of CD4 + and CD8 + lymphocyte counts by the Flow Cytometry device (FCM) (PARTEC, Japan). By employing the colorimetric enzymatic method and the precipitation techniques, the serum level of TG, HDL, and LDL were determined explicitly.

Data were analyzed using SPSS for windows (version 19.0, Chicago, IL). The Pearson correlation was calculated to compare the relationship of parameters between the HIV-positive and HIV-negative groups. The *t*-test was also employed to analyze the relationship between the hematological parameters and other biochemical profiles with CD4 + cell count, CD8 + cell count, and WBC count. Analysis of variances (ANOVA) was the test of choice in assessing the relationships between CD4+, CD8+, and WBC categories (sub-divided into more categories by defining the cell count levels) and other hematological and biochemical parameters. Values were deemed significant at $P < 0.005$ and correlations received their own level of significance at values less than 0.01 or 0.05.

The study was approved by the Research Ethics Committee of the Tehran University of Medical Sciences (TUMS) and informed consent was obtained from each patient before entering the study.

RESULTS

A total of 228 consecutive patients were enrolled in our study, 114 in the case group and 114 in the control group. The mean ± SD of all the variables are summerized in Tables 1 and 2. As mentioned earlier, two groups were similar in terms of sex, age, and other sociodemographic features.

The hematological parameters and biochemistry elements were measured in each patient and were compared between the groups [Tables 1 and 2]. Among the hematological parameters (mean ± SD : HIV negative vs. HIV positive), CD4 + cell count (CD4 + ↓ : 981.37 ± 261.21 vs. 292.59 ± 189.57), CD8 + cell count (CD8 + ↓ : 964.08 ± 267.61 vs. 772.71 ± 380.48), white blood cell count (WBC↓ : 6881.02 ± 1293.76 vs. 5444.28 ± 1999.25), red blood cell count (RBC↓ : 4.89 ± 0.51 vs. 4.34 ± 0.86), hematocrit (HCT↓ : 44.34 ± 2.72 vs. 40.38 ± 5.14), mean corposcular volume (MCV↑ : 92.47 ± 4.26 vs. 94.77 ± 12.93), mean corposcular hemoglobin (MCH↑ : 29.09 ± 1.71 vs. 33.17 ± 5.37), mean corposcular hemoglobine concentration (MCHC↑ : 32.90 ± 1.86 vs. 34.89 ± 1.52), platelet count (PLT↓ : 275.39 ± 81.17 vs. 200.57 ± 79.34), eosinophil count (EOS↑ : 1.71 ± 0.83 vs. 184.03 ± 152.78), and basophile count (BASO↑ : 1.35 ± .716 vs. 25.43 ± 15.52)

Table 1: Pattern of hematological parameters, lipid profiles, and micronutrient elements based on HIV status

Parameters	HIV status	Mean	SD	*P* value
CD_4	HIV negative	981.3772	261.21847	0.000
	HIV positive	292.5965	189.57109	
CD8	HIV negative	964.0877	267.61095	0.000
	HIV positive	772.7193	380.48722	
WBC	HIV negative	6881.0263	1293.76814	0.000
	HIV positive	5444.2895	1999.25713	
RBC	HIV negative	4.8930	.51965	0.000
	HIV positive	4.3498	.86678	
HCT	HIV negative	44.3412	2.72234	0.000
	HIV positive	40.3833	5.14243	
MCV	HIV negative	92.4737	4.26181	0.072
	HIV positive	94.7763	12.93676	
MCH	HIV negative	29.0965	1.71907	0.000
	HIV positive	33.1728	5.37940	
MCHC	HIV negative	32.9035	1.86713	0.000
	HIV positive	34.8965	1.52727	
PLT	HIV negative	275.3947	81.17441	0.000
	HIV positive	200.5789	79.34431	
EOSINOPH	HIV negative	1.7193	.83622	0.000
	HIV positive	184.0351	152.78952	
BASOPHIL	HIV negative	1.3509	.71621	0.000
	HIV positive	25.4386	15.52277	
TRIGELIC	HIV negative	184.9912	21.37342	0.000
	HIV positive	141.7105	85.52107	
CHOLESTR	HIV negative	190.193	30.9447	0.466
	HIV positive	199.026	125.4243	
HDL	HIV negative	63.5000	21.12049	0.000
	HIV positive	44.9737	28.43078	
LDL	HIV negative	120.5351	23.55682	0.000
	HIV positive	88.1228	24.43707	
MG	HIV negative	2.2079	.34670	0.000
	HIV positive	2.7490	.95477	
ZN	HIV negative	97.4211	11.08447	0.000
	HIV positive	149.3246	48.27896	
ALKP	HIV negative	215.4386	57.79320	0.394
	HIV positive	229.0702	160.30478	
P	HIV negative	3.2939	.52987	0.004
	HIV positive	3.6368	1.14330	
ADA	HIV negative	27.3947	16.92650	0.000
	HIV positive	8.9912	4.49286	

*Unites : blood cells : count / micro liter (μl); HCT : %; MCV : femtoliters / cell (fl); MCH : picograms / cell; MCHC : grams / deciliter; TG, CH, LDL, and HDL : mg / dl; MG, ZN, and P: mg / dl ALKP : IU / L; ADA : IU / L

obtained significnat differences between groups ($P < 0.05$). Considering the biochemistry parameters (mean ± SD : HIV negative vs. HIV positive) [Table 2], trigelicerides (TG ↓ : 184.99 ± 21.37 vs. 141.71 ± 85.52), total cholesterol (CH ↑ : 190.19 ± 30.94 vs. 199.02 ± 125.42), high density lipoprotein (HDL ↓ : 63.50 ± 21.12 vs. 44.97 ± 28.43), low density lipoprotein (LDL ↓ : 120.53 ± 23.55 vs. 88.12 ± 24.43), magnesium (MG ↑ : 2.20 ± 0.34 vs. 2.74 ± 0.95), Zinc (ZN ↑ : 97.42 ± 11.08 vs. 149.32 ± 48.27), phosphorus (P↑ : 3.29 ± 0.52 vs. 3.63 ± 1.14), and adenosin deaminase (ADA↓ : 27.39 ± 16.92 vs. 8.99 ± 4.492) were significantly different in HIV-positive patients compared to the controls ($P < 0.05$).

HIV-positive patients were divided into five categories based on the level of the $CD4^+$ cell count per milimeter : less than 50 as category 1, 50 – 100 as category 2, 100 – 200 as category 3, 200 – 500 as category 4, and more than 500 cell count as category 5. A similar division was done for HIV-positive patients based on the CD8 + count (less than 100, 100 – 200, 200 – 500, and more than 500), and WBC count (less than 1200, 1200 – 3500, and more than 3500) with four and three groups, respectively.

According to the five categories of CD4+, statistically significant differences were observed in CD8+, white blood cells (WBC), eosinophils (EOS), and alkaline phosphatase (ALKP) in relation to the CD4+ numbers ($P < 0.05$) [Table 3]. Considering the four categories for CD8+ as a level of division, the hematological variables were compared between the groups; the same was done for three categories of WBC with different levels. The former showed statistically significant differences in CD4+, WBC, platelets (PLT), and basophils (BASO), in relation to the CD8+ numbers, and the latter revealed similar significant differences in CD4+, CD8+, WBC, RBC, hematocrit (HCT), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), and EOS ($P < 0.05$) in relation to WBC count [Tables 4 and 5].

Pearson correlation was also calculated for detecting the association between constant values of CD4+, CD8+, WBC, and RBC, with other constant variables, and were deemed significant at the related levels of < 0.01 or < 0.05. The tables show a positive and significant correlation between CD4+, CD8+, and WBC; RBC and HCT; CD8 + and PLT; EOS, WBC, and RBC; BASO and WBC; ALKP and WBC; and a negative and significant correlation between RBC, MCV, MCH, and MCHC; WBC and MCHC; LDL and RBC; and ALKP and CD4+.

DISCUSSION

Many of blood parameters were assessed in this study to find the impact of HIV infection and the progress of the diseases due to these parameters; with a larger sample size of study population compared to the previous ones; this study could be unique in its type. The hematological parameters as well as lipid profiles and micronutrient elements were assessed in our analysis, with special attention to adenosine deaminase (ADA).

There are sufficient evidences regarding the hematopoietic alterations in HIV-infected patients and its advanced

Table 2: Association between CD4 + categories and mean ± SD of hematological variables in HIV-positive patients

Variable	Category 1*	Category 2*	Category 3*	Category 4*	Category 5*	*P*
CD4	21.00 ± 15.51	76.88 ± 19.11	149.21 ± 149.21	313.06 ± 80.09	620.50 ± 117.59	0.00
CD8	399.55 ± 260.74	727.22 ± 359.41	673.10 ± 326.37	839.93 ± 358.35	866.88 ± 455.64	0.01
WBC	5412.22 ± 3231.15	5243.33 ± 1968.50	4566.84 ± 2245.25	5460.15 ± 1623.19	6435.00 ± 1892.71	0.08
RBC	4.45 ± 0.74	4.64 ± 1.00	3.89 ± 0.83	4.40 ± 0.85	4.45 ± 0.84	0.15
HCT	39.08 ± 3.74	42.00 ± 3.16	37.91 ± 5.76	40.85 ± 5.25	41.29 ± 4.94	0.15
MCV	89.30 ± 12.18	93.32 ± 15.49	99.05 ± 12.06	94.55 ± 12.67	94.45 ± 13.77	0.50
MCH	30.62 ± 5.98	33.22 ± 6.45	34.71 ± 4.82	33.13 ± 5.23	32.91 ± 5.60	0.50
MCHC	34.07 ± 2.54	35.44 ± 1.59	34.96 ± 1.15	34.95 ± 1.41	34.75 ± 1.57	0.40
PLT	150.11 ± 84.26	207.00 ± 91.68	216.47 ± 105.29	197.83 ± 63.89	214.83 ± 83.59	0.30
EOS	320.00 ± 204.14	231.11 ± 151.52	130.52 ± 147.55	168.64 ± 134.74	199.44 ± 156.59	0.02
BASO	32.22 ± 17.87	18.88 ± 6.00	24.21 ± 17.42	24.74 ± 12.91	28.88 ± 21.93	0.35
TG	154.88 ± 89.76	113.88 ± 26.33	122.63 ± 34.76	148.44 ± 94.48	147.11 ± 107.99	0.65
CH	175.66 ± 49.25	188.88 ± 74.88	195.63 ± 54.07	187.10 ± 42.75	258.44 ± 294.72	0.30
HDL	35.55 ± 12.30	49.00 ± 37.40	44.94 ± 17.01	46.47 ± 34.68	42.77 ± 12.79	0.85
LDL	85.55 ± 25.59	87.77 ± 35.14	90.78 ± 25.96	86.91 ± 21.19	90.72 ± 28.46	0.95
MG	2.62 ± 0.76	3.07 ± 1.46	2.39 ± 0.56	2.79 ± 0.94	2.87 ± 1.08	0.38
ZN	152.00 ± 58.78	163.33 ± 43.22	152.05 ± 44.60	143.15 ± 47.31	158.33 ± 53.94	0.66
ALKP	279.44 ± 104.82	334.55 ± 494.27	259.94 ± 132.44	213.52 ± 72.36	169.50 ± 36.59	0.07
P	3.55 ± 0.81	3.60 ± 0.48	3.55 ± 0.55	3.73 ± 1.48	3.47 ± 0.59	0.93
ADA	10.66 ± 3.60	10.66 ± 5.09	8.31 ± 4.43	9.22 ± 4.59	7.27 ± 36.59	0.22

*Categories; 1 : 0 – 50; 2 : 50 – 100; 3 : 100 – 200; 4 : 200 – 500; 5 : > 500

Table 3: Association between CD8 + categories and mean ± SD of hematological variables in HIV-positive patients

Variable	Category 1*	Category 2*	Category 3*	Category 4*	*P*
CD4	21.0000	38.0000	219.96 ± 181.81	320.67 ± 184.41	0.02
CD8	94.0000	152.0000	390.03 ± 77.49	903.52 ± 344.43	0.00
WBC	13100.0000[1]	38.0000[1]	4260.38 ± 1607.76	5694.52 ± 1827.97	0.00
RBC	3.2600	3.9100	4.23 ± 0.84	4.40 ± 0.87	0.46
HCT	32.4000	35.0000	40.89 ± 5.39	40.38 ± 5.04	0.30
MCV	99.4000	89.5000	98.40 ± 12.35	93.68 ± 13.10	0.40
MCH	31.6000	31.5000	34.82 ± 5.42	32.71 ± 5.35	0.36
MCHC	31.8000	35.1000	35.26 ± 1.67	34.81 ± 1.45	0.12
PLT	179.0000	55.0000	155.11 ± 75.96	216.26 ± 74.40	0.00
EOS	240.0000	510.0000	163.84 ± 149.72	185.69 ± 151.74	0.16
BASO	40.0000	70.0000	23.84 ± 13.58	25.23 ± 15.47	0.02
TG	240.0000	73.0000	155.88 ± 108.32	137.08 ± 77.58	0.40
CH	193.000	132.000	178.11 ± 40.83	206.19 ± 142.07	0.74
HDL	37.0000	13.0000	40.11 ± 10.21	46.90 ± 31.93	0.48
LDL	76.0000	79.0000	84.73 ± 20.17	89.39 ± 25.81	0.78
MG	2.5000	2.0200	2.81 ± 1.01	2.74 ± 0.94	0.86
ZN	131.0000	214.0000	146.69 ± 49.25	149.58 ± 48.26	0.57
ALKP	421.0000	397.0000	208.92 ± 115.65	230.97 ± 171.27	0.40
P	4.2000	2.2000	3.28 ± 0.46	3.75 ± 1.26	0.16
ADA	14.0000	13.0000	9.03 ± 5.24	8.87 ± 4.26	0.56

*Categories : 1 : 0 – 100; 2 : 100 – 200; 3 : 200 – 500; 4 : > 500; [1] out of layer data

Table 4: Association between WBC categories and mean ± SD of hematological variables in HIV positive patients

Variable	Category 1*	Category 2*	Category 3*	*P*
CD_4	0	171.94 ± 136.69	315.21 ± 190.07	0.00
CD8	0	479.00 ± 151.31	827.79 ± 385.60	0.00
WBC	0	2935.55 ± 404.68	5914.67 ± 1819.05	0.00
RBC	0	3.80 ± 0.69	4.45 ± 0.86	0.00
HCT	0	37.82 ± 6.60	40.86 ± 4.70	0.02
MCV	0	100.06 ± 10.97	93.78 ± 13.08	0.06
MCH	0	35.77 ± 5.11	32.68 ± 5.31	0.02
MCHC	0	35.63 ± 1.60	34.75 ± 1.47	0.02
PLT	0	169.27 ± 81.16	206.44 ± 78.03	0.07
EOS	0	112.22 ± 84.33	197.50 ± 159.16	0.03
BASO	0	22.77 ± 14.06	25.93 ± 15.79	0.44
TG	0	135.16 ± 61.93	142.93 ± 89.46	0.72
CH	0	181.00 ± 47.69	202.40 ± 135.02	0.50
HDL	0	42.55 ± 8.44	45.42 ± 30.77	0.70
LDL	0	85.05 ± 28.49	88.69 ± 23.72	0.56
MG	0	2.59 ± 0.88	2.77 ± 0.96	0.46
ZN	0	146.33 ± 45.17	149.88 ± 49.04	0.78
ALKP	0	208.88 ± 64.72	232.85 ± 172.41	0.56
P	0	3.24 ± 0.41	3.71 ± 1.22	0.11
ADA	0	9.22 ± 4.75	8.94 ± 4.46	0.81

* Categories : 1 : < 1200; 2 : 1200 – 3500; 3 : > 3

stages of AIDS diseases.[6,8,9,11-13] Anemia, leukopenia, lymphocytopenia, granulocytopenia, and thrombocytopenia are common findings among this population. Bone marrow changes also add to these alterations and show the effect of HIV infection to be more fundamental than a peripheral interference; in fact, pancytopenia is always persistent in advanced stages of HIV infection.[8,9,14,15] However, this is not always that simple, as it has been reported that anemia and other hematological changes occur more severely in some of the endemic regions like southern Africa, rather than regions in the United States,[13] suggesting that more precaution to be applied in interpreting the results.

Dislipidemia, including alterations in the metabolic profiles of blood biochemistry, has also been discussed in the literature; this includes lower triglycerides (TG), HDL, and LDL.[4,7,10] Similar to hematological alterations, the lipid profile also has a complexity of an inter-region pattern of change, as Mondy *et al*. have reported a diminished level of HDL and an elevated level of TG among US HIV-positive population,[16] while Buchacz *et al*. have shown that HIV-positive patients in Uganda have uncommon elevations in their serum levels of TG, LDL, and cholesterol (CH);[17] all these point to a very important lesson, and that is, that the wide spectrum of variation between HIV-related changes around the world, neccessitate close attention in treating HIV-infected patients at each seperated setting.[18] Riddler *et al*. have shown that lipid changes could be divided into two different patterns; one before the initiation of antiretroviral therapy (decreased serum levels of CH, LDL, and HDL) and another pattern of changes would occur afterward (starting to increase the levels of CH, LDL, and HDL, to reach the pre-infection levels after a minmum of three years);[7] thus, a lot more studies are needed to reveal the underlying mechanism of all these inconsistencies, to reach a consensus around this issue. In addition, it would be beneficial to assess the serum levels of antiretrovial medications and metabolites, in association with patterns of lipid profile.

In our study, CD4+, CD8+, WBC, RBC, HCT, and PLT were lower in HIV-positive patients, while MCV, MCHC, EOS, and BASO were significantly higher, compared to the control group. As described earlier, the hematopoiesis change in HIV-infected patients and the bone marrow of these cases have apparently shown significant myelodysplasia and subsequent supression; so it is not far from the mind that the hematopoietic parameters have been diminished in their levels and RBC morphology has been changed similar to the megaloblastic alterations. Thrombocytopenia is one of the greatest manifestations of hematopoiesis impairments in association with HIV;[18-21] however, many underlying mechanisms have been explained with uncertainty in this regard.[11,12] Anemia has been documented to occur in association with HIV infection by one of the following mechanisms: dysfunction of myloid progenitor cells in the bone marrow, antibody secretion against erythroid antigens, and impairment of the precursors' metabolisms.[11] This explains the lower number of RBC counts among HIV-positive patients and an increased MCV in them, as well as, raised MCH and MCHC. Involvment of progenitors in their early stages of division is also suggested by other studies.[22-24] Leukopenia is another hematological manifestation in HIV-positive patients[25] which can be in direct association or inversly related to neutropenia.[26] However, as our population was selected from among the uncomplicated patients referring to the clinic for behavioral disorders, with no serious concerns of infectious disease (i.e., is related to HIV-associated neutropenia), we did not intend to measure the absolute netrophile count (ANC). Basophile and Eosinophil counts were also correlated with HIV infection and CD4+ counts, as this may be due to the increased risk of opportunistic and parasitic infections and dysregulation of the immune system in HIV-infected subjects.

In case of lipid profiles, triglycerides (TG), high density lipoprotein (HDL), and low density lipoprotein (LDL) were lower and total cholestrol was significantly higher in the HIV-positive group; a varying spectrum has been defined for patterns of lipid profile in association with

Table 5: Correlation between hematological parameters, biochemical profiles, and micronutrient elements with CD4 + cell, CD8 + cell, WBC, and RBC count in HIV infected patients

Parameters	Correlation	CD_4	CD8	WBC	RBC
CD_4	Pearson correlation	1	.258**	.299**	.109
	P value	.	.006	.001	.247
CD8	Pearson correlation	.258**	1	.409**	.107
	P value	.006	.	.000	.257
WBC	Pearson correlation	.299**	.409**	1	.105
	P value	.001	.000	.	.265
RBC	Pearson correlation	.109	.107	.105	1
	P value	.247	.257	.265	.
HCT	Pearson correlation	.139	.100	.046	.742**
	P value	.141	.291	.625	.000
MCV	Pearson correlation	-.045	-.061	-.118	-.760**
	P value	.638	.520	.210	.000
MCH	Pearson correlation	-.054	-.069	-.162	-.693**
	P value	.567	.463	.085	.000
MCHC	Pearson correlation	-.046	-.051	-.213*	-.199*
	P value	.628	.591	.023	.034
PLT	Pearson correlation	.105	.271**	.170	-.158
	P value	.268	.004	.070	.094
EOSINOPHIL	Pearson correlation	-.039	.169	.250**	.197*
	P value	.682	.072	.007	.036
BASOPHIL	Pearson correlation	.065	.063	.242**	.038
	P value	.492	.504	.010	.688
TRIGELIC	Pearson correlation	.112	.099	.119	-.011
	P value	.237	.293	.207	.909
CHOLESTEROL	Pearson correlation	.121	-.023	-.029	-.010
	P value	.200	.806	.757	.918
HDL	Pearson correlation	.054	.006	.039	-.125
	P value	.566	.952	.684	.183
LDL	Pearson correlation	.035	-.020	-.008	-.191*
	P value	.713	.829	.935	.041
MG	Pearson correlation	.089	.078	.075	.042
	P value	.346	.412	.428	.656
ZN	Pearson correlation	-.005	-.034	.055	-.089
	P value	.959	.723	.561	.348
ALKP	Pearson correlation	-.239*	.053	.203*	.179
	P value	.010	.578	.030	.057
P	Pearson correlation	.031	.178	.130	.143
	P value	.744	.058	.168	.128
ADA	Pearson correlation	-.149	-.056	.049	-.164
	P value	.113	.551	.607	.082

**Correlation is significant at the 0.01 level, *Correlation is significant at the 0.05 level

HIV infection.[16,17] These reports are even more complexed with initiation of antiretriviral regimens, as this medication shows certain dyslipidemic impacts.[4,7,10] In our study, the complex pattern of lipid profile alterations can be explained by the uncertain pattern of antiretroviral therapies each patient has recieved. Periard *et al.* has also concluded that such patterns can be unique to any different compound that HIV-infected patients are recieving as daily therapies.[4]

Our results also showed that magnesium (Mg), zinc (Zn), and phosphorus (P) were higher in HIV-infected persons. This was in contrast to the previous reports, which revealed with confidence that HIV infection was a cause of micronutrient deficiency, and such supplements should accompany the antiretroviral therapies that the indicated patients were taking.[27-29] Although there were evidences about the toxic and adverse effects of high levels of mineral supplements in HIV-infected individuals,[29] it was of great importance that the deficiency of such elemnts should be wisely approached.[30]

The higher levels of some of these minerals in the serum of HIV-infected patients in our study may be due to the effect of the highly consumed nutritional supplements that are becoming prevalent in developing countries, as the people might domestically have an idea of enriching

the sick people by adding nutritional supplements in their diet. However, this is one of the hypotheses that should be examined by documenting studies. Also it is wise to pay special attention to the higher levels of serum calcium, due to the hyperparathyroidism in HIV-infected heroin addicts;[31] this by a similar mechanism may interfere with the metabolism of body minerals and develop higher levels of blood micronutrients. However, we must notice that this level of abnormality does not evoke an intervention, and it has still remained as a normal range of our referal laboratory. In addition, it has been expressed that HAART is capable of repleting the reservoir of micronutrients within the bodies of HIV-infected patients, especially when observational studies with a large sample size and rational period of follow-up are established.[29] The higher levels of serum micronutrient elements in our study may also be associated with the uncontrolled administration of supplements in the theraputic diets of patients. Before intending to recommend nutritional supplements to the patients suffering from HIV infection, there must be more evidence regarding the benefits of such an approach, including lowering the mortality and transmission rates of HIV infection.[30]

Adenosin deaminase wassignificantlylower in association with HIV infection; previous studies have well described the increased level of ADA in patients suffering from inflammatory processes,[32] infections,[33] immunodeficiency syndromes,[34] and AIDS.[35] Such an inverse correlation has been also detected in association with CD4+ cell count.[36]

Alkaline Phosphatase (another variable among our results) showed an increased level in its serum concentration, but did not recieve statistically significant differences. Activation of lymphocytes was seen to increase the production of ALKP in HIV infection,[37] which was similar to and in line with our results.

As limitations of our study, we should point to the small sample size compared to the larger and multinational studies and the unicentral nature of our investigation; besides, the percise serological measurments along with more attention to the serum levels of more blood elements should be included. Attention should also be paid to the antiretroviral therapies, as these medications are responsible for many of the remaining questions.

As mentioned earlier in this manuscript, further studies should target the exact investigation of viral load and viral activity, the regimen of antiretroviral therapies, and their associations with blood parameters from hematological to metabolic, lipid, and micronutrient profiles, with a larger sample size and in a multicenter setting.

CONCLUSION

Our study showed that like similar studies from the HIV-endemic regions, HIV infection affects hematopoiesis by diminishing the hematological productivity parameters and increasing RBC-related morphology; in addition, we showed a different pattern of lipid profile (decreased TG, LDL, and HDL, and increased CH) and serum micronutrients (elevated concentration of serum trace elements) in our HIV-positive population.

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