HIV AND DECREASED RISK OF MULTIPLE SCLEROSIS: ROLE OF LOW CD4+ LYMPHOCYTE COUNT AND MALE PREVALENCE

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Objectives

Human immunodeficiency virus (HIV) infection has been reported to decrease the risk of developing multiple sclerosis (MS)[1], two diseases with opposite gender prevalence.

The aim of this retrospective case-control study was to compare the number of circulating CD4+, CD8+, CD19+ and natural killer (NK) lymphocytes among HIV and MS patients, and healthy controls.

Materials and Methods

The analysis of immune cell subsets in peripheral blood was performed by flow cytometry using a six-colour single platform immune staining kit. HIV viral load was estimated with real-time PCR testing: if the viral load was below the lower detectable limit of 20 copies/ml the HIV patient was considered "virologic responder"; if the viral load was over the 20 copies/ml, the patient was considered "virologic non-responder".

Statistical analysis was performed by Student's t-test or one-way analysis of variance (ANOVA), and a post-hoc analysis using Bonferroni correction for multiple comparisons.

Results

As expected, both CD4+ cell count and CD4/CD8 ratio were lower while CD8+ cell number was higher in HIV patients compared to MS patients and controls. NK cells were lower in MS patients compared to controls (**Table1**). 18 HIV patients were naïve-untreated, and 40 were HAART-treated including 24 virologic responders and 16 non-responders. 28 MS patients (15 remitting and 13 relapsing) were untreated, and 18 patients(8 remitting and 10 relapsing) were treated with immunomodulatory drugs (interferon-β and glatiramer acetate). Naive HIV patients had a higher CD8+ cell number and both a lower CD4+ cell number and CD4/CD8 ratio ($p<0.0001$) compared to controls (**Table2** and **Fig.1**). HAART-treated HIV patients had a higher CD8+ cell number and a lower CD4/CD8 ratio ($p<0.0001$) compared either to controls, treated and untreated MS groups and a higher CD4+ number with respect to untreated HIV patients and a higher NK cell number compared to treated MS patients. Untreated MS patients had a higher number of CD4+ and CD19+ cells, a higher CD4/CD8 ratio ($p<0.0001$) and a lower number of CD8+ cells as compared to untreated HIV patients and no significant difference compared to controls. Treated MS patients showed a lower number of CD4+, CD8+ and NK lymphocytes compared to those untreated as well as compared to controls. CD4/CD8 ratio was lower in female HIV non-responders and in relapsing MS women compared, respectively, to female HIV responders (0.4 ± 0.1 vs. 1.3 ± 0.2, $p = 0.002$) and remitting MS women (1.8 ± 0.6 vs. 2.3 ± 0.6, $p = 0.02$), and there were no differences in men.

Discussion and Conclusions

On the basis of our results and literature data, we supposed that reported decreasing effect of HIV infection on MS development is likely determined by its immunosuppressive status with a low CD4+ count and by its male prevalence due to different male/female immune characteristics.

References

1. Gold J, Goldacre R, Maruszak H, Giovannoni G, Yeates D, Goldacre M (2015) HIV and lower risk of multiple sclerosis: beginning to unravel a mystery using a record-linked database study. J Neurol Neurosurg Psychiatry 86:9–12. doi: 10.1136/jnnp-2014-307932

Disclosure

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Table 1. Demographic and clinical characteristics, circulating lymphocyte subsets number of participant's groups.

Variable	Healthy controls *n*=31	MS patients *n*=46	HIV patients *n*=58	p value [a]	p value [b]	p value [c]
Females/Males	18/13	36/10	6/52	NS	<0.0001	<0.0001
Age years (mean ± SD)	45.9 ± 9.8	43.0 ± 11.1	43.6 ± 11.8	NS	NS	NS
Disease duration months (mean ± SD)	NA	126.1 ± 81.5	96.7 ± 80.8	NA	NA	NS
CD4 cells/ml (mean ± SD)	870 ± 242	768 ± 405	619 ± 269	NS	0.002	0.05
CD8 cells/ml (mean ± SD)	538 ± 236	392 ± 199	925 ± 374	NS	<0.0001	<0.0001
CD19 cells/ml (mean ± SD)	206 ± 88	243 ± 126	212 ± 117	NS	NS	NS
CD4/CD8 ratio (mean ± SD)	1.8 ± 0.6	2.1 ± 0.8	0.8 ± 0.4	NS	<0.0001	<0.0001
NK cells/ml (mean ± SD)	251 ± 85	185 ± 102	225 ± 116	0.01	NS	NS

[a] p value represents differences between MS patients and Healthy controls; [b] p value represents differences between HIV patients and Healthy controls; [c]p value represents differences between the MS and HIV patients.

Table 2. Circulating lymphocyte subsets number of multiple sclerosis (MS) treated and untreated patients, human immunodeficiency virus (HIV) treated and untreated patients and healthy controls.

Variable	Healthy controls *n*=31	MS patients *n*=46		HIV patients *n*=58	
		Treated *n*=18	Untreated *n*=28	Treated *n*=40	Untreated *n*=18
CD3 cells/ml (mean ± SD)	1464 ± 382	940 ± 443	1286± 563	1688 ± 488	1394 ± 525
CD4 cells/ml (mean ± SD)	870 ± 242	612 ± 298	868 ± 437	699 ± 259	440 ± 200
CD8 cells/ml (mean ± SD)	538 ± 236	310 ± 165	445 ± 203	940 ± 356	890 ± 419
CD19 cells/ml (mean ± SD)	206 ± 88	226 ± 108	253 ± 137	236 ± 122	157 ± 85
CD4/CD8 ratio (mean ± SD)	1.8 ± 0.6	2.2 ± 0.9	2.0 ± 0.7	0.8 ± 0.4	0.6 ± 0.4
NK cells/ml (mean ± SD)	251 ± 85	133 ± 57	218 ± 111	229 ± 111	215 ± 130

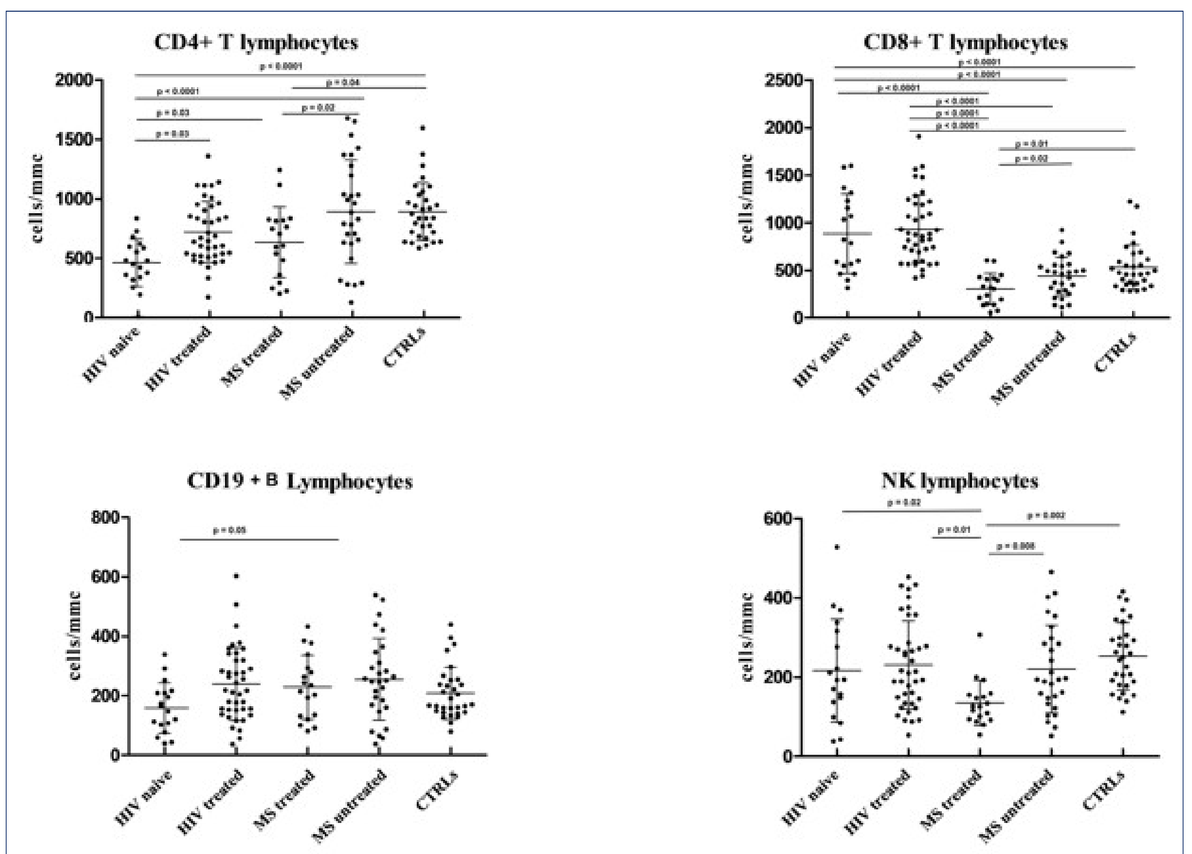

Fig. 1 Comparisons of lymphocyte subsets number (cells/mmc) between healthy controls, HIV-infected naive and treated patients, multiple sclerosis treated and untreated patients. P value refers to Student's t test.