

# Progressive Multifocal Leukoencephalopathy, still a challenge in the combined antiretroviral therapy era

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## Objectives

The aim of our study was to assess prevalence, clinical outcomes and survival in HIV-infected patients diagnosed with **progressive multifocal leukoencephalopathy (PML)** in a Romanian tertiary care facility.

## Methods

Retrospective study on HIV-infected patients hospitalized with PML at Victor Babes Hospital, Bucharest, between January 2006 and December 2018. PML diagnosis was based on **clinical symptoms, neuroimaging, positive CSF PCR-DNA JC virus** and **neuropathology and histology of the brain tissue**. Statistical analysis was performed using SPSS vs. 20.0.

## Results

24.315 HIV-infected patients in active care, annually (2006-2018)

Prevalence: 3.5/1000 PY

87 patients diagnosed with PML

### Characteristics of HIV-infected patients diagnosed with PML

Characteristics	Method	Total	PI	SI	PWIDs	p value
Total	n (%)	87 (100.0)	47 (54.0)	35 (40.2)	5 (5.7)	
<b>▼ Socio-demographic Characteristics</b>						
Age at PML diagnosis (years)	median (IQR)	27 (23, 33)	27 (22, 27)	34 (30, 41)	28 (28, 29)	<0.0001
Age at HIV diagnosis (years)	median (IQR)	22 (11, 31)	11 (8, 15)	32 (26, 41)	28 (27, 29)	<0.0001
<b>▼ Clinical Characteristics</b>						
PML and HIV diagnosed simultaneously	n (%)	25 (28.7)	4 (8.5)	19 (54.2)	2 (40.0)	<0.0001
Previous cART	n (%)	45 (72.5)*	32 (51.6)*	10 (16.1)*	3 (4.8)*	0.001
Infratentorial lesions (brain MRI)	n(%)	25 (28.7)	14 (29.7)	9 (25.7)	2 (40.0)	0.782
<b>▼ Paraclinical Characteristics</b>						
Positive CSF PCR-DNA JCV	n(%)	30 (34.4)	13 (27.6)	13 (37.1)	4 (80.0)	0.059
CD4 cell count/μl	median (IQR)	53 (16, 129)	36 (13, 80)	84 (23, 164)	204 (203, 264)	0.006
Nadir CD4 cell count/μl	median (IQR)	38 (14, 85)	22 (9, 64)	55 (19, 97)	162 (2, 204)	0.007
Plasma HIV-RNA (log <sub>10</sub> copies/mL)	median (IQR)	4.72 (2.92, 5.40)	4.52 (2.47, 5.42)	5.10 (3.77, 5.38)	3.57 (2.64, 4.82)	0.959
CSF HIV-RNA (log <sub>10</sub> copies/mL)	median (IQR)	3.89 (2.71, 4.59)	2.44 (1.60, 4.20)	2.90 (1.60, 4.34)	1.59 (1.59, 1.85)	0.549

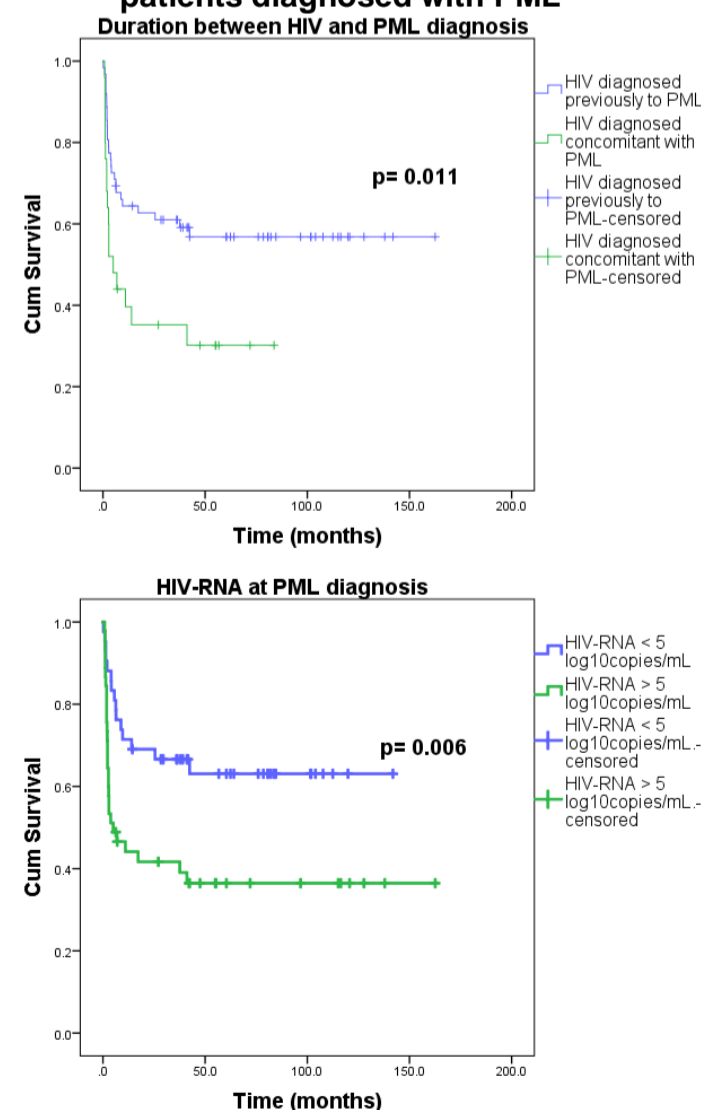
\*out of 62 persons previously diagnosed with HIV; \*\*out of 45 patients previously on ART  
PI = parenteral transmission, during childhood; SI = sexual transmission; PWIDs = people who inject drugs

### Risk factors for high mortality rates in HIV-infected patients diagnosed with PML

	Total n	Mortality rate n (%)	Early mortality rate n (%)	Survival (months) median (IQR)
Total	87	43 (49.4)	26 (29.8)	27.0 (2.7, 68.0)
<b>▼ Modes of HIV Transmission</b>				
Parenteral (childhood)	47	23 (48.9)	12 (25.5)	37.6 (3.2, 80.7)
Sexual Contact	35	18 (51.4)	14 (40.0)	9.6 (1.8, 55.1)
Injecting drug use	5	2 (40.0)	0 (0.0)	37.9 (36.6, 41.0)
p value		0.888	0.119	0.312
<b>▼ Duration between HIV and PML diagnosis</b>				
Concomitant	25	17 (68.0)	12 (48.0)	5.0 (1.7, 41.1)
Prior HIV diagnosis	62	26 (41.9)	14 (22.5)	37.7 (4.0, 82.2)
p value		0.024	0.020	0.011
<b>▼ PML diagnosis status</b>				
Definitive diagnosis	30	17 (56.6)	10 (33.3)	14.2 (2.8, 46.2)
Presumptive diagnosis	57	26 (45.6)	16 (28.0)	28.3 (2.2, 84.5)
p value		0.225	0.393	0.029
<b>▼ CD4 cell count at PML diagnosis</b>				
CD4 < 100/μl	57	31 (54.3)	18 (31.5)	14.4 (2.7, 78.5)
CD4 ≥ 100/μl	30	12 (40.0)	8 (26.6)	36.1 (3.1, 60.3)
p value		0.085	0.267	0.881
<b>▼ Nadir CD4 cell count</b>				
Nadir CD4 < 50/μl	50	31 (62.0)	18 (36.0)	7.8 (2.1, 56.3)
Nadir CD4 ≥ 50/μL	37	12 (32.4)	8 (21.6)	41.0 (6.3, 80.6)
p value		0.008	0.128	0.014
<b>▼ HIV RNA level at PML diagnosis (log<sub>10</sub>copies/mL)</b>				
HIV-RNA > 5.00	33*	21 (63.6)	16 (48.4)	6.3 (2.1, 42.4)
HIV-RNA ≤ 5.00	42*	15 (35.7)	5 (11.9)	40.0 (9.0, 80.7)
p value		0.015	0.001	0.013

\*out of 75 available

### Risk factors for short survival time in HIV-infected patients diagnosed with PML



## Conclusions

PML prevalence was high due to **late diagnosis** and/or **poor adherence to ART**. SI and PWIDs were **diagnosed simultaneously with HIV and PML** in most cases and had more severe immunosuppression, compared to PI. **High HIV viral load at PML diagnosis** was a predictor for short-term survival and increased mortality rate.