No evidence of clinical impact of STIs on seminal HIV burden during successful ART

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1 • BACKGROUND •

- Sexually transmitted infections (STI) are known to increase the HIV shedding in semen of ART naïve patients.
- In the context of an undetectable viremia, both HIV-RNA and HIV-DNA can be detected after 6 months of ART in human seminal fluid.
- Despite this, no risk of HIV transmission is even reported among serodifferent heterosexual and MSM couples in which the HIV-positive partner was using suppressive ART and who reported condomless sex.

2 • AIM •

The aim of this study was to investigate the role of STI in influencing the HIV seminal compartment despite peripheral undetectable HIV-RNA in a cohort of HIV-1 infected patients followed in clinical practice.

3 • METHODS •

30
HIV-1 infected patients in virological successful (viral load<20 copies/mL) for at least 1 year.

15
STI positive
- Case -

15
STI negative
- Controls -

Blood and semen specimens from cases were collected at enrolment and after STI treatment.

Total HIV-DNA

- For each patient, total HIV-DNA has been quantified at enrolment and after STI treatment starting from a pellet of PBMCs/seminal cells. A duplex amplification by ddPCR targeting LTR-5' and housekeeping gene albumin was performed (detection limit of 32 cps/10^6CD4+cells) .
- Quantitative results were then normalized in number of copies per million of CD4+ T cell count for peripheral blood and per million of cells for seminal compartment.

Residual Viremia

- Residual viremia at enrolment and after STI treatment was measured by ddPCR home-made protocol targeting Integrase region. The limit of detection (LOD) was 2 copies/mL.

4 • RESULTS •

Patients' characteristics

	Overall N=30	STI N=15	Control N=15	P value*
Age, years, median (IQR)	35 (30-45)	32 (29-39)	38 (34-48)	0.134
Italians, n (%)	29 (96.7)	14 (93.3)	15 (100.0)	1.00
Risk factor:				
Homosexual, n (%)	25 (83.4)	14 (93.3)	11 (73.3)	0.210
Heterosexual, n (%)	4 (13.3)	1 (6.7)	3 (20.0)	
Vertical transmission, n (%)	1 (3.3)	0 (0.0)	1 (6.7)	
HIV Subtype:				
B, n (%)	22 (73.3)	13 (86.6)	59 (60.0)	
non-B, n (%)	6 (20.0)	1 (6.7)	5 (33.3)	0.130
unknown, n (%)	2 (6.7)	1 (6.7)	1 (6.7)	
Time between enrolment and virological suppression, weeks, median (IQR)	109 (63-162)	122 (71-172)	105 (63-152)	0.430
At HIV-1 diagnosis:				
CD4+T count cells (cells/mm^3), median (IQR)	520 (383-692)	549 (392-742)	459 (420-645)	0.470
HIV-RNA, $\log_{10}$ copies/mL, median (IQR)	4.6 (4.3-5.1)	4.6 (4.4-5.3)	4.6 (4.3-5.0)	0.786
At enrolment:				
CD4$^+$T count cells, median (IQR)	730 (578-992)	676 (576-881)	780 (604-1042)	0.512
CD8$^+$T count cells, median (IQR)	770 (618-941)	772 (626-927)	767 (583-981)	0.806
Sexually transmitted diseases:				
Syphilis, n (%)	10 (33.3)	10 (66.5)	-	
Mycoplasma genitalium, n (%)	1 (3.3)	1 (6.7)	-	
Neisseria gonorrhoeae, n (%)	1 (3.3)	1 (6.7)	-	
Ureaplasma urealyticum, n (%)	1 (3.3)	1 (6.7)	-	
C.trachomatis+M.genitalium, n (%)	1 (3.3)	1 (6.7)	-	
Syphilis+C.trachomatis+U.urealyticum, n (%)	1 (3.3)	1 (6.7)	-	

* Statistically significant differences were assessed by Fisher's exact test and Mann-Whitney Test , as appropriate

HIV-DNA

ID	Total HIV-DNA Peripheral (cps/10^6CD4+T)	Total HIV-DNA Seminal cells (cps/10^6cells)
1 **STI** triple	4547	TND
2 **STI** triple	612	TND
3 **STI** triple	TND	TND
4 **STI** triple	1614	TND
5 **STI** triple	135	TND
6 **STI** triple	763	TND
7 **STI** triple	745	<32
8 **STI** triple	16753	TND
9 **STI** triple	305	TND
10 **STI** triple	TND	TND
11 **STI** triple	671	TND
12 **STI** triple	924	TND
13 **STI** triple	1042	TND
14 **STI** dual	TND	TND
15 **STI** triple	393	TND
1 **Control** triple	6275	TND
2 **Control** triple	3433	TND
3 **Control** triple	1386	TND
4 **Control** triple	2581	TND
5 **Control** triple	254	TND
6 **Control** triple	TND	TND
7 **Control** triple	2560	TND
8 **Control** triple	1157	TND
9 **Control** triple	417	TND
10 **Control** triple	4399	<32
11 **Control** dual	TND	TND
12 **Control** dual	172	<32
13 **Control** dual	456	TND
14 **Control** dual	TND	TND
15 **Control** dual	512	TND

TND: target not detected

- Peripheral total HIV-DNA was detectable in 24 patients (80%), with a median (IQR) value of 614 (163-1851) cps/10^6CD4+cells.
- Seminal total HIV-DNA was detectable only in 3 patients (10%, 1 case and 2 controls).
- In all three cases with a quantification <32 cps/10^6CD4+cells.

The **six** patients with **TND** HIV-DNA in peripheral compartment showed also **TND** HIV-DNA in the seminal compartment.

RESIDUAL VIREMIA

- Peripheral and seminal HIV-RNA were detectable in 19 (63%) and 18 (60%) patients, respectively with a median (IQR) of 2.8 (<2.0-4.4) and 5.4 (2.3-9.3) cps/mL.
- In both compartments, residual HIV-RNA never exceeded the 20 cps/mL.

The exception of 2 patients, 1control (congenital infection) and 1 case (co-infected with M.genitalium and C. trachomatis).

7 out of 30 patients (23.3%) showed a seminal HIV-RNA positivity despite the peripheral HIV-RNA negativity

5 of them were STI pts

ID	Residual Viremia Blood plasma (cps/mL)	Residual Viremia Seminal plasma (cps/mL)
1 **STI** triple	TND	3.5
2 **STI** triple	TND	TND
3 **STI** triple	<2	TND
4 **STI** triple	4.4	4.4
5 **STI** triple	<2	2.3
6 **STI** triple	TND	12.2
7 **STI** triple	3.1	TND
8 **STI** triple	<2	5.5
9 **STI** triple	TND	TND
10 **STI** triple	TND	TND
11 **STI** triple	9.0	55.8
12 **STI** triple	3.0	5.4
13 **STI** triple	TND	6.6
14 **STI** dual	3.6	9.0
15 **STI** triple	TND	TND
1 **Control** triple	7.5	6.1
2 **Control** triple	<2	TND
3 **Control** triple	4.0	TND
4 **Control** triple	TND	8.5
5 **Control** triple	<2	TND
6 **Control** triple	TND	TND
7 **Control** triple	TND	TND
8 **Control** triple	2.8	TND
9 **Control** triple	2.7	10.4
10 **Control** triple	TND	<2
11 **Control** dual	2.7	<2
12 **Control** dual	2.7	<2
13 **Control** dual	10.4	39.2
14 **Control** dual	5.7	<2
15 **Control** dual	<2	3.5

TND: target not detected

Residual Viremia pre-post STI treatment

ID	Residual Viremia in seminal plasma (cps/mL) Pre-treatment	Post-treatment
1 **STI** triple	3.5	TND
2 **STI** triple	TND	TND
3 **STI** triple	TND	-
4 **STI** triple	4.4	16.5
5 **STI** triple	2.3	TND
6 **STI** triple	12.2	TND
7 **STI** triple	TND	TND
8 **STI** triple	5.5	-
9 **STI** triple	TND	TND
10 **STI** triple	TND	TND
11 **STI** triple	55.8	TND
12 **STI** triple	5.4	-
13 **STI** triple	6.6	-
14 **STI** dual	9.0	-
15 **STI** triple	TND	-

TND: target not detected

- 9 STI cases were analysed at enrolment and after antibiotic treatment.
- Among these, 4 (44.4%) maintained undetectable seminal HIV-RNA.
- Only one (11.1%) experienced a seminal HIV-RNA increase to 12.1 cps/mL.
- 4 (44.4%) showed a reduction (-3.4, -12.2, -2.3, and -55.8, respectively).
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5 • CONCLUSIONS •

These preliminary data show that successful combined antiretroviral treatment (3DR or 2DR) avoids the presence of HIV-DNA in the seminal cells in the majority of patients, maintaining HIV-RNA in seminal compartment at non-relevant levels, despite STI and independently by drug regimen.

6 • REFERENCES •

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7 • CONTACT •

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