FACTORS ASSOCIATED WITH VIRAL REBOUND POST BLIP IN PATIENTS FROM A COMMUNITY HIV CLINIC

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BACKGROUND

Blips are temporary detectable increases in the HIV viral load (VL) that occur after therapy has effectively suppressed the virus to an undetectable level. The etiology of viral blips is multifactorial, contributing factors include random laboratory variation, ongoing replication, decreased ARTadherence and the release of virus from viral reservoirs. The association between blips and viral failure remains unclear.

OBJECTIVES

The objectives of this study included the calculation of prevalence of viral blips alongside the clinical and demographic characterization of the patients that presented this phenomenon in an inner-city HIV clinic in north Philadelphia between 2014-2018. Other objectives included the determination of prevalence of viral rebound in these patients and the search of factors associated to this outcome.

METHODS

The study was performed at the Immunodeficiency Clinic of the Albert Einstein Medical Center, an urban tertiary teaching hospital in North Philadelphia.

Operational definitions:
Blip: single detectable VL $\leq$ 500 copies/mL which appears between two undetectable VL measurements.
Viral rebound: post blip VL $\geq$ 200 copies/mL that was not followed by an undetectable viral load.

Data collection and analysis:
Retrospective chart review was done of the patients of the Immunodeficiency Clinic between 2014 and 2018 to obtain sociodemographic and clinical characteristics including the immuno-virologic data of the patients that met the definition of viral blip. The outcome studied was virologic rebound post blip.

A descriptive analysis was used to describe the study patient population. A bivariate analysis was performed using Chi-square test to measure the association between relevant patients' characteristics and viral rebound. To evaluate the relationship of VR and other factors, a logistic regression model was performed and odds ratio (OR) and its 95% confidence intervals (CI) were calculated.

RESULTS

Of a total of 666 patients, 225 (33.7%) had at least 1 blip. 59% were male and 41% were female. The majority were African American (84.4%). Sixty seven percent were heterosexuals and 25.7% were MSM. Analyzing CD4 counts at the moment of blip, 68% had $\geq$500 cells/mm³. The average value of the blips was 85 copies/mL with 48.8% of the patients having a blip between 20-50 copies/mL. Most of the patients were on INSTIs (49.5%) followed by NNRTIs (35.6%). Of the 225 patients, 148 had at least 1 year of follow up post-blip. Those who were followed for less than 1-year post-blip were not included in the statistical analysis to find potential factors associated with VR. Thirty-two (21.6%) patients developed rebound. The multivariate analysis showed that older age, being male and having a higher blip value were factors associated to increased likelihood of VR. Factors associated to decreased likelihood of rebound were the use of NNRTIs at blip and an HIV transmission factor that was not heterosexual sex (MSM and IDU).

TABLE 1:
Characteristics of patients with blips

CHARACTERISTICS	NUMBER OF PATIENTS (%)
GENDER	
Male	133 (59.1)
Female	92 (40.9)
RACE/ETHNICITY	
African American	190 (84.4)
Latino	23 (10.3)
Asian	2 (0.9)
White	9 (4)
Other	1 (0.4)
HIV RISK FACTOR	
Injection drug user	13 (5.8)
Men who have sex with men	151 (67.1)
Heterosexual sex	58 (25.8)
Perinatal	2 (0.9)
Transfusion	1 (0.4)
MAGNITUDE OF BLIP (copies/mL)	
20-50	110 (48.9)
51-100	60 (26.7)
101-200	35 (15.5)
>200	20 (8.9)
CD4 at BLIP (cells/m³)	
<200	7 (3.1)
200-500	65 (28.9)
501-1000	105 (46.7)
>1000	48 (21.3)
NUMBER OF BLIPS	
1	165 (73.3)
2	49 (21.8)
3	11 (4.9)
HAART AT BLIP	
INSTI	112 (49.8)
PI	18 (8)
NNRTI	80 (35.6)
PI + INSTI	7 (3.1)
Other	8 (3.5)
STI/HCV coinfection at blip	
STI	16 (7.1)
HCV	13 (5.8)
No coinfection	196 (87.1)

TABLE 2:
Characteristics of patient population

VARIABLE	REBOUND	NO REBOUND	TOTALS	P-VALUE[a]
GENDER				
Male	24 (75.0)	68 (58.6)	92 (62.2)	
Female	8 (25)	48 (41.4)	56 (37.8)	0.0908
Totals	32 (100)	116 (100)	148 (100)	
AGE (years)				
<=40	8 (25)	20 (17.2)	28 (18.9)	
41-60	19 (59.4)	70 (60.4)	89 (60.1)	0.5082
>60	5 (15.6)	26 (22.4)	31 (21)	
Totals	32 (100)	116 (100)	148 (100)	
RACE/ETHNICITY				
Black	26 (81.3)	92 (80.2)	119 (80.4)	
Caucasians	2 (6.2)	6 (5.1)	8 (5.4)	
Hispanics	3 (9.4)	15 (12.9)	18 (12.2)	0.8187
Asians	1 (3.1)	1 (0.9)	2 (1.3)	
>1 race	0 (0)	1 (0.9)	1 (0.7)	
Totals	31 (100)	116 (100)	148 (100)	
HIV RISK FACTOR				
Heterosexual	22 (68.8)	72 (62.1)	94 (63.5)	
MSM	8 (25)	32 (27.6)	40 (27)	
IDU	2 (6.2)	10 (8.6)	12 (8.1)	0.8100
Perinatal	0 (0)	2 (1.7)	2 (1.4)	
Totals	32 (100)	116 (100)	148 (100)	
AGE AT BLIP				
20-29	1 (3.1)	9 (7.8)	10 (6.8)	
30-39	7 (21.9)	11 (9.5)	18 (12.1)	
40-49	11 (34.4)	26 (22.4)	37 (25)	0.1274
50-59	8 (25)	45 (38.8)	53 (35.8)	
>60	5 (15.6)	25 (21.5)	30 (20.3)	
Totals	32 (100)	116 (100)	148 (100)	
BLIP (copies/ml)				
20-50	11 (34.4)	64 (55.2)	75 (50.7)	
51-100	11 (34.4)	30 (25.8)	41 (27.7)	
101-200	7 (21.9)	16 (13.8)	23 (15.5)	0.2053
>200	3 (9.3)	6 (5.2)	9 (6.1)	
Totals	32 (100)	116 (100)	148 (100)	
HAART AT BLIP				
INSTI	16 (50)	48 (41.4)	64 (43.2)	
PI	7 (21.9)	9 (7.7)	16 (10.8)	
NNRTI	6 (18.7)	54 (46.5)	60 (40.5)	
NRTI	0 (0)	1 (0.9)	1 (0.7)	0.0212[b]
PI + INSTI	3 (9.4)	3 (2.6)	6 (4.1)	
PI NNRTI	0 (0)	1 (0.9)	1 (0.7)	
Totals	32 (100)	116 (100)	148 (100)	
CD4 AT BLIP				
<200	1 (3.1)	6 (5.2)	7 (4.7)	
200-500	12 (37.5)	31 (26.7)	43 (29.1)	
501-1000	16 (50)	54 (46.6)	70 (47.3)	0.3542
>1000	3 (9.4)	25 (21.5)	28 (18.9)	
Totals	32 (100)	116 (100)	148 (100)	
COINFECTION WITH SYPHILIS OR HCV				
(1) Syphilis	4 (12.5)	7 (6.0)	11 (7.4)	0.2530[b]
(2) HCV	4 (12.5)	4 (3.5)	8 (5.4)	0.0669
Any of (1), (2)	7 (21.9)	9 (7.8)	16 (10.8)	0.0469

(a) Measure of the association between patient characteristics and VL Rebound (Chi-square test);
(b) Measure of the association between patient characteristics and VL Rebound (Fisher exact test);

TABLE 3:
Comparison of means between rebound and non rebound patients.

VARIABLE	REBOUND			NO REBOUND			P-VALUE[a]
	(N)	MEAN	SD	(N)	MEAN	SD	
Age	32	49.5	11.5	116	51.6	12	0.1857
Age blip	32	47.4	11.1	116	50.0	12.1	0.1004
First VL (log 10)	32	4.2	1.3	116	3.7	1.4	0.1180
First CD4	32	304.4	231.5	116	385.4	342.5	0.3576
Blip (log10) (copics/ml)	32	1.9	0.4	116	1.7	0.3	0.0405
CD4 at blip	32	624.8	263.4	116	718.0	374.9	0.2596
Number of blips	32	1.4	0.6	116	1.5	0.6	0.4597

(a) Comparison of the mean between Rebound and No Rebound using Mann-Whitney test

TABLE 4:
Multivariate Analysis on the Relationship of VL Rebound and Sociodemographic and Clinical Variables

VARIABLES	ODDS RATIO (OR)	P-VALUE	95% CONFIDENCE INTERVAL (CI)
Age	0959	0.0492	0.920-1.000
Male (ref: female)	3.393	0.0450	1.027-11.201
African American (ref: others)	1.415	0.5854	0.406-4.927
MSM/IDU (ref: heterosexual)	0.230	0.0189	0.067-0.784
INSTI (ref: PI)	0.295	0.1159	0.065-1.351
NNRTI (ref: PI)	0.092	0.0054	0.017-0.495
Coinfection Syph/HCV(ref: No)	3.037	0.1114	0.773-11.922
Value at Blip (log10)	5.544	0.0176	1.349-22.783
CD4 at blip	1.000	0.7751	0.998-1.002
Number of blips	0.8000	0.6066	0.343-1.868
First CD4	1.000	0.9473	0.998-1.002

CONCLUSIONS

The variables that were found to be associated to viral rebound could help guide clinicians during the surveillance of patient's with blips. Further research in larger prospective cohorts would help clarify the association of these variables with viral failure in patients with blips.