

von Willebrand Factor Propeptide to Antigen Ratio: Evidence of Endothelial Activation in HIV Infected Pregnancy

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INTRODUCTION

An increased incidence of venous thrombo-embolism (VTE) has been observed in human immunodeficiency virus (HIV) infected pregnant women in the era of antiretroviral therapy (ART).

The extent to which endothelial activation contributes to this increased risk of VTE specifically among virologically- suppressed HIV-infected pregnant women has not been studied.

The plasma ratio of von Willebrand factor (VWF) propeptide to VWF antigen, which declines in normal pregnancy, has been identified as a useful marker of endothelial activation.

AIM

To assess the VWF propeptide to VWF antigen ratio as a marker of endothelial activation in all three trimesters of pregnancy and its relationship with HIV viral load (VL) and ADAMTS13

METHOD

A cross-sectional analysis was performed in 89 HIV infected virologically suppressed patients on ART for 5 [7] years, 63 HIV infected patients with VL >50 copies/ml and 85 matched HIV negative women (Table 1.). VWF propeptide and VWF antigen were measured in the first (6-12 weeks), second (13-26 weeks) and third trimesters (27-39 weeks). Results were correlated with multimer patterns, performed using 0.65% agarose gel, and ADAMTS13 antigen, activity and antibody levels. Clinical and laboratory data were analyzed using Statistica 13.2 software (California, USA) and SAS 9.1 software (Cary, North Carolina, USA).

The study protocol was approved by the ethics committee of the University of the Witwatersrand (M-181018).

RESULTS

VWF propeptide to antigen ratio was increased, in the first, second and third trimester, in the HIV infected group with VL>50 copies/ml and the HIV infected virologically suppressed group as compared to the HIV negative group (p<0.05) (Table 2.).

Increased high molecular weight multimers were observed in the HIV infected groups, despite only a mild reduction in ADAMTS13 activity as compared to the HIV negative group (p<0.001) (Fig 1.).

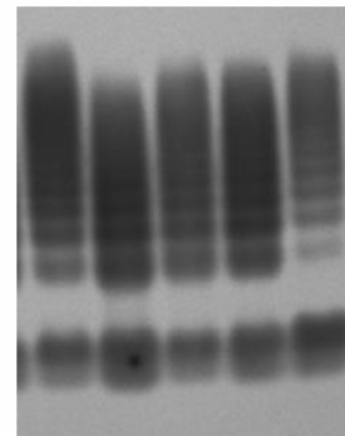
No correlation was observed between VWF antigen or VWF propeptide and ADAMTS13 activity.

Characteristic	HIV negative	HIV VL <50 copies/ml	HIV VL >50 copies/ml	p value
Demographics				
Age	31.0 ± 6.0	34.0 ± 6.0 ***	32.0 ± 6.0	<0.001
Parity	1.0 [1.0]	2.0 [2.0] *	2.0 [2.0]	0.008
BMI	28.3 ± 5.6	27.6 ± 5.8	27.4 ± 6.0	0.545
Laboratory characteristics				
White cell count	7.9 ± 2.0	7.7 ± 2.4 **	6.7 ± 2.1 *	0.012
Hemoglobin	124.5 ± 12.8	119.3 ± 14.7	114.5 ± 16.6 **	<0.001
Platelet count	254.7 ± 74.0	249.2 ± 66.0	261.3 ± 99.3	0.719
Delivery characteristics				
Termination of pregnancy	0 (0)	5 (5.6)	0 (0)	0.058
Live births	78 (91.8)	79 (88.8)	61 (96.8)	
Intra-uterine fetal death	7 (8.2)	5 (5.6)	2 (3.2)	
Gestational age delivery	39.0 ± 2.0	37.0 ± 4.0 *	38.0 ± 2.0	0.040
Birthweight	2914.6 ± 1102.0	2315.5 ± 1283.1 **	2596.5 ± 1136.8	0.004
Outcome				
VTE	0 (0)	0 (0)	0 (0)	-

Table 1. Demographics and clinical, laboratory and delivery characteristics of the three study groups

Characteristic	Trimester	HIV negative	HIV VL <50 copies/ml	HIV VL >50 copies/ml	p value
Log VWF antigen	First	4.7 ± 0.4	5.0 ± 0.4 *	5.0 ± 0.4	0.021
	Second	5.1 ± 0.3	5.2 ± 0.3 *	5.2 ± 0.3	0.042
	Third	5.3 ± 0.3	5.4 ± 0.4	5.4 ± 0.4	0.038
Log VWF propeptide	First	5.1 ± 0.4	5.4 ± 0.4 ***	5.4 ± 0.4 ***	<0.001
	Second	5.3 ± 0.4	5.8 ± 0.4 ***	5.6 ± 0.4	<0.001
	Third	5.4 ± 0.6	5.7 ± 0.7 *	5.6 ± 0.8 *	0.001
VWF pp to Ag ratio	First	1.4 ± 0.6	1.7 ± 0.7	1.9 ± 0.9 *	0.030
	Second	1.3 ± 0.4	1.7 ± 0.4	1.7 ± 0.9	0.033
	Third	1.2 ± 0.3	1.6 ± 0.5	1.6 ± 1.1	0.035
ADAMTS13 antigen	First	67.0 ± 23.7	61.0 ± 23.0	63.6 ± 24.1	0.591
	Second	65.6 ± 19.0	67.0 ± 24.2	67.8 ± 21.8	0.940
	Third	67.3 ± 14.4	69.4 ± 24.1	67.3 ± 20.8	0.908
ADAMTS13 activity	First	84.5 ± 31.4	55.1 ± 25.2 ***	53.6 ± 23.3 ***	<0.001
	Second	92.9 ± 27.3	62.7 ± 30.1 ***	64.6 ± 29.2 **	<0.001
	Third	96.1 ± 24.4	71.5 ± 29.9 **	63.4 ± 26.5 ***	<0.001
ADAMTS13 autoantibodies	First	4 (12.9)	3 (8.6)	5 (22.7)	0.296
	Second	4 (14.8)	4 (14.8)	5 (26.3)	0.551
	Third	5 (18.5)	3 (11.1)	5 (22.7)	0.534

Table 2. Comparison of von Willebrand Factor associated parameters between the three study groups



1 2 3 4 NPP

Figure 1. Electrophoresis gel images of high molecular weight multimer and low molecular weight multimer patterns in HIV infected with virological suppression (patient 1), viral load (VL) >50 copies/ml (patient 3), and normal pooled plasma

CONCLUSIONS

HIV infected virologically suppressed participants showed persistent endothelial activation in all three trimesters of pregnancy.

Future research should focus on whether endothelial activation contributes to the excess risk of pregnancy related VTE.

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