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Hemostasis in HIV Infected Individuals

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Abstract
With the introduction of cART, HIV infection is slowly evolving into a chronic disease. HIV-related thrombocytopenia is the most common hemostaticdisorder. In addition, there are some abnormalities in the fluid phase of the coagulation cascade which can produce bleeding or thrombosis in the HIV patient. The most common are thrombocytopenia, prolonged prothrombin time, prolonged partially activated thromboplastin time, the production of a lupus anticoagulant and anticardiolipin antibodies, and several abnormalities in the natural-occurring anticoagulants. The thrombotic thrombocytopenic purpura (TTP) recently associated with HIV has a clinical presentation and treatment alternatives that closely resemble those for the classical disease. This study was conducted to know the pattern of these hemostatic abnormalities among PLHA's. Our study showed most of hemostatic abnormalities occurred with advanced stage of disease which was stastistically significant too. Several thrombotic events were noted in the form of ischemic stroke and DVT, but no clinically significant bleeding manifestations. The knowledge of these hemostatic abnormalities and its early identification in the HIV seropositive patient allows a more rational care of these patients.
Keywords: *cART, hemostatic disorder, PLHA, thrombocytopenia, TTP, DVT, lupus anticoagulant.*

Introduction

The advent of HAART in HIV/AIDS has improved the mortality and reduced the morbidity of HIV infected individuals, as measured by the incidence of opportunistic infections. This lead to the evolution of HIV into a chronic disease and extended the lifespan of PLHAs. Thus, many complications, either due to HIV infection or HAART related, came into light among which the hemostatic abnormalities have gained their significance in recent years.

Materials and Methods

A cross-sectional study was conducted on 100 patients with HIV infection either attending ART clinic or those who were inpatients in Rajiv Gandhi Government General Hospital, Chennai to evaluate the hemostatic status of HIV infected individuals irrespective of their ART status and to study the association of CD4 count, WHO staging, cART intake, and comorbidities independently with the hemostatic parameters. 50 belonged to the pre-ART group and 50 belonged to the ART

group. The analysed hemostatic parameters were platelet count, prothrombin time, activated partial thromboplastin time, plasma fibrinogen and serum lactate dehydrogenase. Special investigations like D-Dimer and Lupus anticoagulant were done when required. The hemostatic parameters were evaluated in all individuals irrespective of their clinical symptoms.

Discussion and Results

Thrombocytopenia was noted among 51 PLHA's in our study but there was no statistically significant correlation with either CD4 count or WHO staging of disease. Significant co-morbid illnesses were identified in all PLHA's with moderate-severe thrombocytopenia and 58.5% of PLHA's with mild thrombocytopenia. The thrombocytopenia in otherwise asymptomatic patients might be attributed to HIV infection itself or due to drugs.

Prothrombin time was prolonged in 48% patients in our study and aPTT in 22% of our patients. The higher incidence of PT prolongation could be attributed to alcoholic hepatic dysfunction. All patients with aPTT prolongation had significant co-morbid illnesses. The increased coagulation parameters got corrected with normal plasma except the one who presented with stroke and found to be positive for LAC.

The most interesting feature noted in our study was the striking absence of bleeding diathesis despite the hemostatic derangements. But thrombotic manifestations were noted in eight patients in the form of ischemic stroke, DVT and Cavernous sinus thrombosis. This leads us to the possible influence by HIV infection & ART on the antithrombotic factors like protein C, protein S, anti-thrombin III and others which needs to be distinctly delineated. Most of the studies have shown significant changes in the presence of antiphospholipid antibodies and the lupus anticoagulant; deficiencies of protein C, protein S, heparin cofactor II, and antithrombin; and increased levels of von Willebrand factor and D-Dimer and these abnormalities correlate with the severity of HIV-associated immunosuppression as measured by CD4+ cell counts and the presence of infectious or neoplastic diseases associated with HIV infection.

Thrombocytopenia vs Who Staging

THROMBOCYTOPENIA	WHO STAGES			
	I	II	III	IV
Mild (1-1.5lakhs)	17(41.46%)	2(4.87%)	9(21.95%)	13(31.7%)
Moderate (0.5-1lakh)	-	2(22.23%)	1(11.12%)	6(66.67%)
Severe (<50,000)	-	-	-	1(100%)

In our study, majority of thrombocytopenia noted in stages I& IV. There was no statistical significance between thrombocytopenia and WHO staging (p value-0.066).

Prothrombin Time vs Who Staging

PROTHROMBIN TIME	WHO STAGING			
	I	II	III	IV
Normal	26	1	9	12
Prolonged	11(22.91%)	2(4.16%)	9(18.75%)	26(54.16%)
Reduced	3	1	-	-

Majority of prolonged PT was noted in patients with stage IV disease. There was statistical significance for PT with WHO staging (p value-0.015) by Chi square test.

aPTTVs Who Staging

Aptt	WHO STAGING			
	I	II	III	IV
Normal	35	3	12	22
Prolonged	1(4.54%)	1(4.54%)	6(27.27%)	14(63.63%)
Reduced	4	-	-	2

Majority of patients with prolonged aPTT were noted in advanced stages III and IV disease. There was statistical significance for aPTT with WHO staging (p value-0.008).

Fibrinogen vs Who Staging

FIBRINOGEN	WHO STAGING			
	I	II	III	IV
Normal	25	2	8	16
Increased	-	-	1(25%)	3(75%)
Reduced	7(19.44%)	2(5.55%)	9(25%)	18(50%)

Majority of fibrinogen derangements are noted among advanced stages. There was statistical significance between fibrinogen and WHO staging (p value-0.018) by Chi square test.

LDH vs Who Staging

LDH(U/L)	WHO STAGING			
	I	II	III	IV
Normal	21	2	11	21
Increased	-	1(12.5%)	1(12.5%)	6(75%)
Reduced	19	1	6	11

About 75% of patients with raised LDH belonged to stage IV. There was statistical significance between WHO staging and LDH (p value-0.005) by student t test.

Analysis of hemostatic parameters between patients on ART & non-ART

	PRE-ART		ART		P value
	Mean	SD	Mean	SD	
Platelet	1.76	1.08	1.52	0.47	0.156
PT	13.93	2.68	13.1	1.89	0.077
aPTT	35.5	10.29	33.5	7.72	0.281
Fibrinogen	203.53	85.58	193.02	51.02	0.458
LDH	250.12	116.95	264.12	139.47	0.588

The above analysis shows that there is no statistical significance between hemostatic parameters of patients on ART & without ART.

Analysis of hemostatic parameters with WHO staging

Parameters	STAGE I		STAGE II		STAGE III		STAGE IV		P value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Platelet	1.67	0.44	0.97	0.28	1.62	0.64	1.67	1.2	0.455
PT	12.39	1.33	12.27	1.7	14.2	2.07	14.49	2.8	0.000
aPTT	29.67	4.4	33.42	4.28	38.08	10.09	38.14	10.48	0.000
LDH	219.3	46.17	422.2	361.8	241.8	99.45	286.8	145.2	0.005

From the above analysis, it is shown that there is statistical significance of PT, aPTT, LDH with WHO staging.

Conclusion

The emphasis of our observation is that effective prophylactic measures against thrombosis in PLH As need to be incorporated in routine therapeutic strategies. This provides a strong rationale for careful prospective studies to evaluate the prevalence, pathogenesis, and risk factors associated with the development of thromboembolic complications in patients with HIV infection.

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